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HOSPITAL INFECTIONS AND THEIR CONTROL: PITFALLS IN THE INTERPRETATION OF STATISTICAL DATA*

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The problem of intra-hospital infection has been the subject of world-wide concern, and even controversy, during the past decade. The shift in emphasis to the institution as a nidus of spreading pathogens is, in part, the natural outcome of an abating conflict with the once insurmountable infections originating in the community. These far-reaching changes, promulgated by a revolution in therapeutic approach, gave hopes that the antibiotics would someday end the struggle with all death-dealing bacteria. It was soon found that these drugs are not omnipotent.

INCIDENCE AND NATURE OF HOSPITAL INFECTIONS

Many investigators have reported a profound change in the character and number of infections since the introduction of antibiotics (1–3). Chiefly, there has been growing concern that drug-resistant strains of staphylococcus are rising (4), perhaps due to interference with the usual interspecies relationships (5). Moreover, it has been observed that the growth, or resistance, of certain organisms is directly correlated with the antibiotic agents persistently employed in a given area (4, 6, 7), and that a diminution in resistance may occur with discontinuance of the drug (6). Finland *et al.* (7) have shown that the incidence of the staphylococcic strains resistant to various forms of antibiotic therapy appears to be much greater in hospitalized patients than in either out-patients or in recently admitted patients not previously treated with these drugs.

Moreover, Finland (8) has reported that although the percentage mortality from bacteremias showed a decided decline at Boston City Hospital following the introduction of sulfonamides, an upsurge (though less marked) was apparent from 1947 to 1957. The total number of bacteremias, fatal and non-fatal, steadily increased after 1935. This occurred in spite of the fact that hospital admissions showed no proportional rise.

In addition to antibiotic therapy and its abuse, there seem to be other factors which have altered the bacterial incidence of infections in recent years. Such, for example, are the increasing age and debility of the hospital population and

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the introduction of ever-more hazardous surgery, both of which may explain the varying incidence of sepsis from institution to institution and from year to year. When data are based on relatively homogeneous groups, as in "uncomplicated" surgery, it appears that the rate of sepsis in clean incisions, as reported from one of our outstanding hospitals, has not increased from 1937 through 1957 (9). Viewing the situation from another angle, it is but small comfort that neither has the rate *improved* in twenty-one years!

Barnes and his associates (9) based this investigation upon the important observation that the rates of sepsis fluctuate as a greater or lesser proportion of operations include diverse risks. Their premise was borne out for a group of 9,447 "uncomplicated" operations (inguinal herniorrhaphies and abdominal hysterectomies), in which the incidence of sepsis remained approximately 4.3 per cent over the twenty-one year period. The rate did not perceptibly sway, possibly due to compensatory factors, even with the introduction of antibiotic agents.

When a more divergent group of patients undergoing a less benign form of surgery was considered by the same workers (10), results were, predictably, not as constant. Thus, in 3,000 subtotal gastrectomies, the incidence of postoperative sepsis varied for the periods 1932 through 1940 (16 per cent), 1941 through 1953 (4.1 per cent), and 1954 through 1958 (9.4 per cent). The highest rate of postoperative sepsis (that observed prior to 1941) was not attributed, as might be expected, to lack of an as yet unexplored arsenal of antibiotic drugs, but rather to the lesser availability of blood transfusions. Sepsis, again on the rise after 1953, could have well been due, as the authors suggest, to an altered population of patients and an increasing number of emergency subtotal gastrectomies.

An increasing number of wound infections, particularly of the more serious sort, was noted by Howe (4) for the five-year period from 1949 through 1953. Here the heterogeneity of surgical cases and the alteration in hospital population were fairly marked. From the data, it is also clear that the ward service at the hospital had a rate of wound infection about three times as high as that of the private service. The difference in the morbidity and mortality due to infections, between ward and private services, has been attributed by Guthorn *et al.* (11) to the more advanced age of the patients and the multiple complications encountered on a ward service (11).

In considering the problem of hospital infections, as much interest has been focused on the nature of the infecting organisms, as on degree of infection. Of the common Gram-positive bacteria, *Staphylococcus aureus* has been the most stubborn offender. *Candida albicans*, a mycotic organism, and the "enterobacteria" or "aerobic Gram-negative" pathogens normally found in the human body have also caused increasing concern since the introduction of the newer drug therapy (1, 2, 8). The enterobacteria include chiefly *Escherichia coli*, *Aerobacter aerogenes*, *Pseudomonas aeruginosa*, *Proteus vulgaris* and *Bacillus alcaligenes* (1, 2). Most of these pathogens are relatively resistant *in vitro* to the widely available antibiotics and respond poorly to adequate therapy (1, 8). Serious infection due to Gram-negative organisms, producing bacteremia and even bacteremic shock, has been reported (12–14).

PITFALLS IN INTERPRETATION OF STATISTICS

A comprehensive study of the extent of these pathogens in hospital infections was undertaken by Finland and his associates (1) at the Boston City Hospital; it included seven turn-point years, selected in relation to the introduction of the various anti-microbial agents. Finland *et al.* found an increasing percentage of *Staphylococcus aureus* in the autopsy material obtained and cultured in the period from 1935 through 1957 and, furthermore, its rise as a pure or predominant organism. This was considered "a very crude index of the increasing significance of Staph. aureus as a major or contributing cause of death" (1). On the other hand, it could be interpreted as a reflection merely of the relative decline of other organisms, such as the hemolytic streptococcus and the pneumococcus, with the introduction of techniques effective in their control. The parallel finding of a growing proportion of *Staphylococcus aureus*, as well as of the enterobacteria, in the various cultures from hospital infections may be viewed similarly.

More debatable are the absolute increases that Finland *et al.* (1) noted in the numbers of patients with infections due to *Staphylococcus aureus* and enterobacteria, since it is not clear whether all infections were consistently cultured over the period of study. If an increasing number of cultures were undertaken each year without consistent correlation to the number of infections, then an observed rise in the incidence of a given pathogen could be more apparent than real. Such a circumstance could cloak even a virtual fall in the frequency of infection with staphylococcus and the enterobacteria. Thus, in the event that cultures have not been uniformly or totally accomplished, it might prove invaluable for investigators to compare the percentage of specific infections *per cultures* made, rather than draw inferences on the basis of any shift in absolute numbers.

Rogers (2) of the Cornell University Medical Center, in 200 consecutive autopsies of medical cases during the pre-antimicrobial two-year period from 1938 to 1940, found a greater number of fatal infections than in a corresponding 200 autopsies during a nine-month period from 1957 to 1958. Fifty-four per cent of the subjects of the earlier group had died with an infection, and in 28.5 per cent, the infection was a major factor in the death. On the other hand, in the period of antibiotic usage, 29 per cent had had an infection, but in only 14 per cent did it play an important part in death. One may wonder, however, whether the choice of material in two periods of decidedly differing length was proportionately representative of the seasons. Among medical patients, at least, the seasons may be expected to exert an influence in the transmission of infection.

On the basis of his material, Rogers reported an actual decline in pneumococcal and streptococcal fatalities from the pre-antibiotic to the later antibiotic period (2). He noted no significant change—certainly no increase—in the number of cases in which staphylococcus played a contributing role. It should be emphasized that this occurred in spite of a decline in the total number of all infections. The enterobacterial and mycotic infections showed a rise from the one era to the other, and this increase together with an essentially unaltered

number of staphylococcus infections supported "the impression that antimicrobials have not dramatically altered the risk of, or mortality resulting from, *endogenous* infections arising in *sick*, *hospitalized* patients." (Our italics.)

It can also be deduced from Rogers' work that in the later period the number of hospital-acquired infections increased *relative* to those originating in the community, at least among the patients who died in the hospital.[1] However, this could have been due to a marked decline in infections on the outside which necessitated hospitalization, probably as the result of effective antibiotic therapy. Furthermore, an inspection of Rogers' data shows that although the proportion of hospital-to-outside-acquired infections increased among the cases studied, there was a drop in the over-all number of hospital-acquired infections, from 47 among 200 cases in the preantimicrobial period to 38 among 200 in 1957–1958. As may have been anticipated, antecedent disease was much less common among the earlier group, being absent in 40 per cent, as compared with only 7 per cent in the later period.

In spite of reports of the serious role of *Staphylococcus aureus* itself in nursery and surgical units, there is a conviction in some quarters that epidemics of staphylococcic infections have not been a problem on medical services in the absence of influenza (2, 15). Vogel *et al.* (16) reported an epidemic of hospital staphylococcus on an adult medical ward, which flared in the presence of influenza. This disease, due to the 52/52A/80 strain of *Staphylococcus aureus*, originated from 3 patients with heavy and chronic skin infection. A second or respiratory phase ensued when Asian influenza appeared within the hospital. In a very short time, staphylococcal pneumonia developed in the same area. As the influenza disappeared, the epidemic strain of staphylococcus spread violently throughout the hospital, causing a third phase, chiefly of skin disease. The spread followed closely the movements of heavily contaminated patients in the hospital. Resistance to antibiotics developed rapidly. Six of the 14 fatalities occurring in relation to the epidemic were among cancer patients, and in 5 of these 6, the infection was the major cause of death. The remaining 8 deaths occurred in patients with other debilitating disease. Rigid measures brought the epidemic under control.

LITERATURE ON THE CONTROL OF HOSPITAL INFECTIONS

The means of preventing hospital-acquired infections has been the subject of many studies. Ralph Adams *et al.* (17) suggest chiefly an environmental approach. They state that good housekeeping is the best investment in the hospital control of infection; that nine-tenths of the transmissions of infection occur through the air or by way of the skin. Hudson and his associates (18) describe a bacteriocidal treatment of air for hospitals, wherein four-fifths of the bacteria in the air can be removed by an air and fomite system (with bacteriocidal air filters); they suggest that sterilizing or bacteriocidal agents be liberally used in cleaning solutions. Chemically treated plastic coverings for sterilized pillows and mattresses have also been recommended (19).

[1] This was a study based upon autopsy findings.

Kresky and Elias (20) and others (16) stress the culturing and bacteriophage-typing of staphylococcus. In the control of infection among personnel, bi-monthly nasal and throat swabs are recommended, but shifting of nurses or other help throughout the hospital is deplored (20).

Special measures are important in the nursery and in maternity sections (20, 21). It is noteworthy that epidemics arising from these areas do not remain excluded from the community (20, 22). Periodic cultures of material from infants in the nursery and the isolation of infants with skin or other infections are advised (20). A shorter hospital stay for mothers and infants is advocated (20, 21). Farrer *et al.* (21) find that compulsory rooming-in of infants and mothers, more than removal of nasal carriers of infection, is a most effective technique in avoiding dissemination of infection. This could possibly be due to the more rigid regulations for rooming-in.

Most investigators concur regarding the limitation of antibiotic therapy, or its discreet use, in selected cases (19, 23). Its effectiveness in the prevention of pneumonia in patients with acute heart failure has been questioned (24). Moreover, antibiotic prophylactic treatment in surgery does not appear to be beneficial in preventing postoperative infection (25), including sepsis in clean wounds (9). Instead of antibiotics, germicides have been advocated for reducing the urinary-tract infections that occur after instrumentation (26).

Meanwhile, new weapons are being sought with which to eliminate the problem of hospital infections. The answer may be found ultimately, in spite of the present disillusionment, in more diverse and more effective antibiotics. Part of this dream shows some promise of fulfillment in the form of new penicillin preparations (such as BRL 1241) which appear to be effective against present resistant staphylococcal strains and certain other pyogenic organisms (27–29). However, unless man's ingenuity in creating effective antibiotics exceeds the rate of natural selection in providing new resistant strains of pathogens, the drive to prevent infections by other means must continue vigorously.

INCIDENCE AND NATURE OF INFECTIONS FOR THE YEAR 1959 AT MOUNT ZION HOSPITAL

In 1959 all postoperative infections[2] (constituting half of the postoperative complications[2]) occurred among 4.4 per cent of the surgical patients at Mount Zion Hospital (Table 1). Fifty-four per cent of these infections were wound sepsis and appeared in 2.4 per cent of the surgical patients. This incidence of wound infection is about the same as the 2.3 per cent average derived from Guthorn's data on private and ward patients (11). Howe (4) found an average of 3.98 per cent for major and minor wound infections in the year 1953, and of 2.85 per cent for those considered only major. Barnes *et al.* (9) reported an approximate 4.3 per cent incidence of wound sepsis in selected types of surgery, studied over a period of years. The differences in these rates of incidence are small, particularly in view of the wide divergence in the types of surgery, in the age and debility of the patients, and the nature of hospital facilities and

[2] These numbers do not include more than one infection or complication per patient.

TABLE 1

Postoperative Infections, 1959

	Number	Incidence
Total operations	6,432	
Total patients with postoperative complications	573	9% of patients operated on
Total patients with postoperative infections	285	4.4% of patients operated on 50% of patients with postop. complications
Total wound infections	153	2.4% of patients operated on 54% of patients with postop. infections
As the only complication	122	
With other infection	13	
Total deaths with postoperative complications	35	0.5% of patients operated on 6.1% of patients with postop. complications
Of these, complication an infection (hospital-acquired)	19	6.7% of patients with postop. infections

care of the patient. Another important factor is the length of the period of observation, which may vary according to duration of hospitalization and to subsequent management (9, 11).

At Mount Zion Hospital, 6.7 per cent of all the postoperative infections[2] were a contributing factor in death but, as can be seen from Table 2, these occurred either in aged or severely debilitated patients or in those undergoing high-risk surgery. The infections in 4 of those who died (Patients #20–23) could not be considered definitely postoperative or hospital-acquired. In Patient #20 a brain abscess appeared to have resulted from otitis media rather than from surgery. Patient #21 entered the hospital with perforation of the cecum after suffering multiple traumatic injuries; Patient #22 was admitted with a bilateral tubo-ovarian abscess following a septic abortion; peritonitis developed in both cases. In Patient #23, pneumonia occurred six days after discharge from the hospital, or a total of twenty-three days after valvotomy for mitral stenosis.

Among the medical patients, more than twice as many of the staphylococcus aureus infections originated in the community than in the hospital. Among the surgical group, more infections were hospital-acquired rather than outside-acquired. The data on the patients who died are more limited, but again suggest a *greater role of the hospital in the origin of staphyloocccal infection among surgical patients.* This difference is to be expected when one considers the divergence in types of ailments necessitating hospitalization on the medical and surgical services.

TABLE 2

Postoperative Infections in Patients who Died 1959

Patient No.	Age (yrs.)	Diagnosis, Surgery	Infection
1	64	Carcinoma colon; colectomy; other pathology	Peritonitis
2	73	Sarcoma sternum (biopsy); leiomyosarcoma uterus; other pathology	Pneumonia
3	73	Fracture femur (nailed); cardiac failure; pulmonary embolus	Bronchopneumonia
4	56	Obliterans arteriosclerosis; midthigh amputation; aortic (abdom.) thrombus	Bronchopneumonia
5	82	Cholelithiasis; cholecystectomy; congestive heart failure	Pneumonia
6	80	Prostatic hyperplasia; retropubic prostatectomy; bilat. vasectomy; pulmonary embolus	Urinary-tract infection
7	70	Diverticulitis; colectomy; acute hemorrhagic pancreatitis	Peritonitis; pneumonia; wound infection
8	87	Hiatal hernia repair; pulmonary embolus; other pathology	Urinary-tract infection
9	68	Parkinson's disease; thermal lesion; arteriosclerotic heart disease	Intracerebellar abscess; bronchopneumonia
10	73	Carcinoma colon; colectomy; pulmonary infarct; other pathology	Bronchopneumonia
11	57	Carcinoma rectum; abdominoperineal resection	Enterocolitis bacteremia; wound infection
12	77	Esophageal diverticulitis; resection; hypertensive heart disease; cardiac failure	Wound infection
13	63	Adenocarcinoma rectum; resection; myocardial infarction; other pathology	Bronchopneumonia; hemorrhagic cystitis
14	89	Fracture hip; pulmonary embolus	Decubitus ulcers; septicemia
15	67	Duodenal ulcer; vagotomy; pyloroplasty; cholecystectomy	Bronchopneumonia
16	"Elderly"	Abdominal carcinoma with invasion; exploratory laparotomy; other pathology	Suppurative parotitis; pneumonia; empyema
17	77	Bronchiogenic carcinoma; lobectomy; other pathology	Empyema
18	45	Mitral stenosis; valvotomy	Subacute bacterial endocarditis
19	72	Infiltrate lingula; pneumonectomy; multiple lung abscesses; coronary occlusion	Bronchopneumonia
20*	70	Otitis media; carotid angiogram; lymphoma; other pathology	Brain abscess; otitis media
21*	49	Multiple traumatic injuries; Steinmann pins; perforation of cecum; subarachnoid hemorrhage	Peritonitis; bronchopneumonia
22*	29	Bilat. tubo-ovarian abscess; exploratory laparotomy; oophorectomy; cardiac arrest (septic abortion)	Peritonitis
23†	53	Mitral stenosis; valvotomy; cardiac failure	Pneumonia

* Infections could not be considered hospital-acquired.

† Borderline case: infection developed six days after leaving hospital, on the twenty-third postoperative day.

The ratio of *Staphylococcus aureus* to other organisms cultured from wound infections (approximately two-thirds of which were the various enterobacteria) was 6 to 5. This is close to Guthorn's ratio of 25 *Staphylococcus aureus* to 20 "mixed flora" infections (11). *Candida albicans* was rare as a pathogen in wound infection at Mount Zion Hospital.

In 1 instance, a postsurgical intracerebellar abscess (Table 2, # 9), in which the invading organism was *Staphylococcus aureus*, responded to antibiotic therapy. One month later it flared anew, but this time *Aerobacter aerogenes* and *Bacillus proteus* had replaced the original pathogen and the abscess did not respond to treatment.

The obstetrics department at Mount Zion Hospital showed a remarkable record for low incidence of hospital infections in 1959. Infections among the newborn were either negligible or absent, and only 1.5 per cent of the maternity patients had hospital-acquired infections, all rapidly controlled. There were no deaths associated with hospital-acquired infections. This paper does not include the possible hospital-acquired infections which might become manifest after discharge from the institution.

A study of the rules and regulations of the obstetrics department, generally more strict than elsewhere, demonstrates the reason for the relatively negligible extent of serious hospital infection in the obstetrics division, and for the absence of epidemic spread. Employees are not permitted to visit patients in other areas of the hospital. Visitors are strictly limited with regard to numbers, visiting hours, age (children under 16 years are not allowed) and the presence of any infection. Infected expectant mothers are excluded from the obstetrics floor; infants with any infection are isolated in a "suspect" nursery. Even more stringent rules govern the rooming-in mothers. Sterile procedures usually reserved for the nursery are included for the rooming-in mother, and visitors are even more restricted than for the other maternity patients.

RECOMMENDATIONS FOR PREVENTION OF HOSPITAL INFECTIONS[3]

1. Staphylococcal infections, including those of skin and respiratory tract, enterobacterial infections and influenza should be treated with *strict isolation* techniques, as they are all contagious diseases. Staphylococcus may become lethal and should be approached with as much care as meningitis.

2. Aged and debilitated patients should routinely receive the benefits of the reverse isolation technique[4], because they are most susceptible to the devastating effects of staphylococcus and similar pathogens.

3. Cultures should be made of any suspected infected lesion, as well as of any drainage from surgical wounds. If the culture shows staphylococcus, coagulase studies and sensitivity tests should be made.

4. Effective antibiotics should be reserved for selected resistant infections, and withheld from general use in the hospital.

[3] This is a modified version of our recommendations to the Patient Care Committee at the Mount Zion Hospital, based upon this study, and including specific suggestions from members of other departments.

[4] Isolation technique protecting *the patient* from outside contamination.

5. Shifting of nurses and other employees throughout the hospital should be avoided, and hospital personnel with infections should be removed from contact with patients.

6. Visitor's privileges should be reviewed and limited according to the hazards of the service.

7. Sterile techniques should be vigorously enforced in the surgical units.

8. Catheterization should be kept to a minimum, and when necessary, performed by a team of trained personnel, with appropriate antiseptic measures.

9. A committee composed of members of the departments of bacteriology, medicine, surgery, nursing, housekeeping and administration should meet bimonthly to evaluate hospital infections.

10. Nurses on each floor, as well as admitting office personnel, should file cards on every infectious patient either entering or within the hospital, for review by the hospital infection committee.

11. New bacteriocidal plastic substances should be investigated in order to test their practicality when applied to telephones, door knobs and other hospital fixtures, as well as medical examining instruments.

SUMMARY

The introduction of ever more radical surgery, the acceptance of an increasingly aged and debilitated hospital population, and the use of more potent and toxic drugs necessitate a correspondingly greater hospital responsibility. It is emphasized that staphylococcal infections, including those of the skin and respiratory tract, enterobacterial infections and influenza are all contagious diseases and should be treated with *strict isolation* techniques. Specific recommendations for other stringent preventive measures in controlling hospital infection are also included.

The literature on the incidence, nature and control of hospital infection, as well as the role of antibiotics, is discussed. Certain statistical pitfalls in evaluating the changing pattern of infecting organisms are disclosed. For example, the reported rises in the incidence of infections with *Staphylococcus aureus* and the enterobacteria could be merely a reflection of the decline in infections with other organisms such as the hemolytic streptococcus and pneumococcus, following the introduction of therapy effective in their control. Any reported change in the absolute number of infections due to a specific pathogen may be misleading, so long as the number of cultures obtained do not consistently parallel all infections observed in a given institution.

The incidence of postoperative infections on a surgical service in Mount Zion Hospital for the year 1959 was 4.4 per cent; approximately half of these infections were in wound incisions. In wound cultures, the ratio of *Staphylococcus aureus* to other pathogens (two-thirds of which were enterobacteria) was 6 to 5. Of the postoperative infections, 6.7 per cent were a contributing factor in death, but these occurred in aged, severely debilitated patients or in those who underwent high-risk surgery.

The data indicate that the hospital plays a greater role in the origin of staphylococcal infection among surgical patients than among medical patients, but this

difference can be attributed to the divergent nature of the ailments necessitating hospitalization on these two services.

The stringency of regulations on the obstetrical service apparently accounted for an almost negligible incidence of infection among mothers and newborns in the hospital.

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MEASUREMENT OF PSYCHOLOGIC FUNCTION IN GERIATRIC PATIENTS

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The Home and Hospital where this study was made is a 350-bed facility that has been in existence for more than sixty-five years. The average age of the patients has increased by 10 years in the past twenty years and is now 82. Problems change with increasing age, not only with regard to the treatment of pathologic conditions but also with regard to the maintenance of mental health. More and more frequently we hear such questions as: What is normal in a population with an average age of 82 years? How does this population differ from one in which the average age is 72 years? If we could know what constitutes normal behavior for a given age group, we should be more able to judge abnormal behavior.

Existing psychologic tests are not satisfactory. As recently as 1958, James E. Birren (1), an authority on psychologic testing in old age, stated: "Research on old age is still in an undeveloped stage." The results of standard intelligence tests are often misleading, especially if they are based on verbalization in such patients. Of more practical importance is the amount of judgment these patients retain. We all know the old man who still recites Latin and talks intelligently about philosophical problems but who cannot remember anything about the present.

A series of tests is needed for measuring psychologic function in the elderly. As Vinson (2) stated in 1952: "If the clinician is to be successful in his effort to rehabilitate the patient he must first understand the nature of psychobiological decline and later the limitations in terms of impairment of function. Only then is he in the position to assist the patient in accepting his limitations as imposed by the ageing process."

Methods are needed by which not only trained clinical psychologists, but practitioners as well, can determine the level of psychologic function so that the great numbers of old people who present problems can be reached. This work is a first attempt to attain a better understanding of functions in old age (particularly the ability to judge), so that geriatric patients can be treated more adequately.

MATERIAL AND METHODS

Subjects

The initial group for the present study comprised 100 guests of the Masonic Home and Hospital in Wallingford, Connecticut. They were chosen largely on the basis of their willing-

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TABLE 1

Age and Sex of Subjects

Age (yrs.)	Females	Males	Total
65–69	2	0	2
70–79	11	7	18
80–89	20	17	37
90–	2	1	3
Total	35	25	60

TABLE 2

Occupations of the 60 Men and Women (or Husbands of the Women) According to the Minnesota Scale, Compared with the Data of the 1920 U. S. Census When the Current Population was Aged 29 to 52

Class	Type of Occupation	This Study	1920 Census
		(%)	(%)
I	Professional	5	3
II	Semi-professional, managerial	13	5
III	Clerical, skilled, retail business	26.6	14
IV	Farmers	5	19
V	Semi-skilled; minor business	30	27
VI	Slightly skilled	6.6	19
VII	Day laborers	5	
VIII	Unclassified	8	

ness to be tested, and all were both mentally and physically able to cooperate in the series of psychologic tests. On the basis of their responses to the Rorschach test, 9 were classified as "normal", 30 as "intact presenile", 39 as "medium presenile", and 22 as "deteriorated presenile."

Of these 100 subjects, 60 were chosen for further testing (3–20). This selection was made, not on the basis of the degree of psychologic intactness or deterioration but rather on the grounds of willingness, cooperativeness and the presence of enough visual and auditory acuity to make further participation in the study practical.

The 60 subjects thus selected included 35 females and 25 males. Ages ranged from 69 to 92, with a mean age of 80 for women and 83 for men. Median ages were 80 for women and 85 for men (Table 1).

These old people were of all levels of social status and ability (Minnesota Occupational Scale) but, in comparison with the total population of the United States, the higher levels were somewhat more frequently represented, as shown in Table 2.

Tests

In spite of the seeming intactness of certain areas, good vocabulary, reasonably good memory and apparent social adequacy, many elderly persons seem to be functioning psychologically at approximately a preschool level, at least in the areas where they cannot utilize previous experiences. Therefore, preschool or early school-age tests may yield a better indication of the exact level of performance and possible functional adequacy than the type of adult test presently being administered. Moreover, in order to measure more effectively the decreasing levels of effective performance in elderly subjects, the clinician

TABLE 3

Clinical Classification and Ages of Subjects

Category	No. of Subjects			Mean Age (yrs.)		Age Range	
	Female	Male	All	Females	Males	Females	Males
Normal	7	0	7	76.28	—	69–81	—
Intact presenile	13	11	24	78.92	82.18	69–85	74–89
Medium presenile	10	6	16	83.90	82.17	71–90	76–91
Deteriorated	5	8	13	84.00	84.37	77–92	78–87
Total	35	25	60				

needs to understand the successive steps in the deterioration of any given function. These steps may often occur in the reverse order of their development in childhood.

The Rorschach test has proved to be useful in drawing definite distinctions between levels of personality deterioration. Therefore, we have used the nomenclature of this test in defining normal, intact presenile, medium presenile and deteriorated states. On the basis of the Rorschach responses, 7 subjects in the group of 60 were in the normal category, 24 in the intact presenile, 16 in the medium presenile, and 13 in the deteriorated category (Table 3). In only 2 instances did subsequent testing with other procedures fail to support this initial classification.

After classification on the basis of the Rorschach responses, the subjects underwent the following series of *preschool or early school-age tests*:

1. Gesell Cubes: tower of 10, bridge, gate, 10-cube steps.
2. Gesell Copy Forms: circle, square, triangle, rectangle with diagonals, diamond.
3. Gesell Incomplete Man.
4. Monroe Visual I.
5. Monroe Visual III.
6. Wechsler Intelligence Scale for Children (WISC): vocabulary, information, comprehension, arithmetic, similarities, digits.
7. Lowenfeld Mosaic.[1]

Specific instructions for the Gesell Cube test are given by Gesell *et al.* (12, 13). Materials are 10 red wooden one-inch cubes. The subject is asked to build a tower of 10 and to copy (not imitate) a bridge of 3 cubes, a gate of 5 cubes, and a 4-step flight of stairs made from 10 cubes.

Materials for the Gesell Copy Forms test are simply a circle, cross, square, triangle, rectangle with diagonals and a diamond, inked in black on white cards measuring 8½ x 5½ inches. The subject is given a card and asked to copy the form on a piece of paper.

Materials for the Gesell Incomplete Man test (3, 12) consist of a letter-size sheet of green paper on which is stamped in black ink the outline of a man having one arm and hand, one leg and foot, one ear, one nose, one mouth, no eyes, hair on only one side of the head, a neckline on one side, and half a necktie. The subject is asked: "What is this?" If he does not name the figure as a "man" or "person," he is told what it is. In either event, he is asked to "finish the man."

The Monroe Visual I test (19) consists of a set of 12 cards, on each of which is printed a simple geometric form. The subject is shown these cards, one at a time, and is asked to indicate which of two forms printed on an accompanying sheet resembles the one shown on the card.

The Monroe Visual III test (19) is more difficult. The subject is shown 4 white cards,

[1] This is the only test (besides the Rorschach test) which is given to children at all ages from 2 years through 16 years.

on each of which are printed in black ink 4 geometric forms in horizontal alignment. Each card is exposed for 10 seconds and the subject is asked to copy from memory what he has seen on the card.

The Wechsler Intelligence Test for Children is described fully in the manual of that name by David Wechsler (20).

The Lowenfeld Mosaic test (18) consists of a box of 456 plastic pieces, 1/16 of an inch thick, in 5 different shapes (square, diamond and 4 triangles—equilateral, right-angled, isosceles and scalene) and in 6 different colors (black, green, yellow, red, white and blue). There are 48 squares, 72 equilateral triangles, 96 diamonds, 96 isosceles triangles, and 144 scalene triangles. The subject is presented with this box of pieces and a white tray covered with a piece of paper 10¼ x 12⅜ inches in size. He is shown the different kinds of pieces and is asked to make something with them on the paper.

RESULTS

Response to individual tests

Rorschach. Since subjects were originally separated into 4 groups on the basis of the Rorschach response, it was not surprising that, as Table 4 indicates, mean values for Rorschach scores in these groups show a marked deterioration of response in the descending order of the categories.

The clearest Rorschach clue to the level of functioning is perhaps found in the qualitative aspects of the response (7). Nevertheless fairly clearcut distinctions between the groups can be seen, at least for certain scoring variables, in Table 4. The number of responses declined steadily, and there was a sharp drop in the deteriorated subjects. The number of refusals, conversely, increased steadily.

TABLE 4

Comparative Rorschach Scores for Each of the 4 Groups

(mean scores)

	Normal	Intact Presenile	Medium Presenile	Deteriorated
N	15.43	13.04	11.06	7.00
Refusals	0.55	0.55	1.59	3.15
M	1.85	1.37	0.94	0.46
FM	1.00	1.50	0.88	0.30
m	0.71	0.96	0.69	0.15
F(C)	0.43	0.96	0.69	0.38
FC	0.28	0.08	0.06	0.07
CF	1.00	0.48	0.69	0.31
C	0.00	0.00	0.00	0.07
sC	1.14	0.56	0.72	0.46
A%	63.43%	64.58%	51.19%	69.15%
H%	14.43%	17.00%	15.06%	11.22%
No. anatomy R	0.43	0.41	0.25	0.61
No. content R	4.40	3.62	3.62	1.91
W%	48.00%	46.46%	48.87%	56.92%
D%	51.43%	47.87%	44.18%	39.38%
Dd%	1.00%	5.66%	6.68%	2.69%
F%	63.57%	58.29%	63.56%	76.00%
F+%	84.86%	85.33%	80.51%	60.04%

With minor exceptions, all types of movement (human, animal, inanimate) fell off steadily and paralleled deterioration, with human movement responses being virtually absent in the most seriously deteriorated group. The number of color responses also decreased steadily until there were virtually no reactions to color in the most deteriorated subjects. Variety of content, too, declined with increasing deterioration. An increasing proportion of all responses were global or whole responses.

The percentage of responses determined by form alone increased steadily (except for a drop in intact presenility); conversely, the percentage of correct responses to form fell sharply. Conspicuous in the most deteriorated group (as seen also in children 5 years of age and younger) was the fact that F % was higher than F+ %.

Gesell Cubes. As Table 5 indicates, all normal and nearly all intact presenile subjects built correctly the tower of 10, the bridge, the gate and the 10-cube steps; therefore, this test obviously does not discriminate effectively between these two groups. However, medium presenile subjects consistently failed to make the 10-cube steps. This failure suggests that any person so failing is below the level of intact presenility. Deteriorated patients failed all of the cube tests except the tower of 10. Such a failure is one of the clearest indications of deterioration given by the present series of tests, and any substantial failure in the cube test appears to be one of the clearest indicators of true deterioration.

Gesell Copy Forms. As with the cubes, both normal and intact presenile subjects succeeded in all the sub-tests. Though occasional failures appeared among the medium presenile subjects, this group, too, held up to the extent that more than half the subjects succeeded in copying forms. Only in the deteriorated group did this pattern break down to the extent that deteriorated elderly subjects failed with both the copy diamond and copy divided rectangle with diagonals. Such a failure supports failure in the cube test as an indication of marked deterioration.

Gesell Incomplete Man. As Table 5 indicates, the mean number of parts added to the man by normal elderly subjects was 8.57, which is typical of a 7-year-old level of response. Intact presenile subjects added 7.87 parts, which is typical of a 5-year-old level of response. Medium presenile subjects added 6.31 parts, but the deteriorated subjects added only 3.39 parts—a typical response of a 4-year-old child.

Differential diagnosis in this test depends more on qualitative factors (such as the angle, placement and length of arm and leg; number, size and placement of hair; type of eye) than strictly on such quantitative considerations as the number or nature of parts added. The evaluation of qualitative factors requires considerable familiarity with this test. However, as seen in Table 5, addition of such basic parts as the arm, finger, leg, foot, hair, eyes, ear and neck suggests that any subject so responding is probably still within the *normal* classification. Omission of only the foot indicates the intact presenile state; omission of the eyes indicates the medium presenile state. Responses are almost completely absent in the deteriorated subjects, who usually add only a very poor-quality arm, leg and one other part.

TABLE 5

Comparative Scores on Gesell and Monroe Tests

Test	Normal (7 Subjects)	Intact Presenile (24 Subjects)	Medium Presenile (16 Subjects)	Deteriorated (13 Subjects)
Gesell Cubes (% correct)				
Tower	100%	84%	80%	60%
Bridge	100%	94%	86%	36%
Gate	100%	89%	80%	27%
Steps	100%	75%	26%	9%
Gesell Copy Forms (% correct)				
Circle	100%	100%	68%	77%
Cross	100%	100%	88%	77%
Square	100%	100%	75%	61%
Triangle	100%	96%	75%	53%
Rectangle	100%	100%	62%	23%
Diamond	100%	87%	56%	15%
Monroe Visual I				
Mean score (% correct)	12%	10.96%	10.20%	4.69%
Monroe Visual III				
Mean score (% correct)	8.93%	2.77%	0.83%	0.92%
Gesell Incomplete Man				
Mean No. of parts	8.57	7.87	6.31	3.39
Hair	6; uneven	6; too short	none	none
Eyes				none
Ear	good placement	variable	variable	none
Arm				
placement	correct	correct	correct	correct or none
length	correct	correct	correct	variable
direction	correct	correct	correct	correct or none
fingers	correct	correct	correct	none
Leg				
placement	correct	too far out	correct	correct
length	too short	correct	too short	too short
direction	too straight	too straight	none	variable
Neck	neckline only	bow	none	none
Parts made:	arm, finger, leg, foot, hair, eyes, ears, neck	arm, finger, leg, hair, eyes, ears, neck	arm, finger, leg, hair, ear, neck	leg, arm & one other

Monroe Visual I. This test is relatively easy for normal, intact presenile and even for medium presenile subjects. As Table 5 shows, even in these last two groups, subjects responded correctly to as many as 10+ out of the possible 12 forms. Deteriorated subjects, however, failed this test signally. Thus failure in Visual I supports failure in the Gesell Cube test and the Copy Form test in classifying a subject as deteriorated.

Monroe Visual III (Fig. 1). With this test, the breakdown of response comes

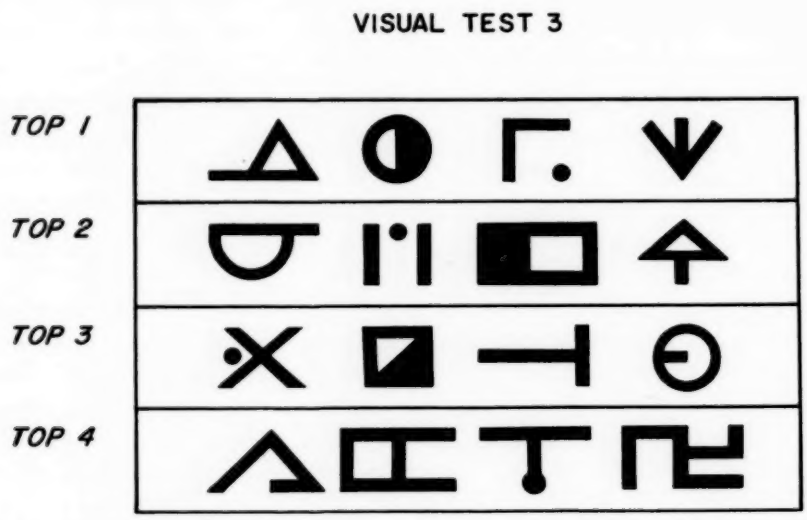

FIG. 1. Example of chart for Monroe Visual Test III. Each line is shown to the subjects for 10 seconds. This test seems difficult, but the ability to copy 2 in 4 figures (50 per cent) is apparently a normal performance indicative of a satisfactory degree of mental competence.

much earlier. As Table 5 shows, Visual III was one of the most difficult tests in this series. Scores fell off sharply from a mean of 8.93 for the normal subjects with 47 per cent correct responses (adequate at the 8 or 9-year age level), to 2.77 with only 35 per cent correct responses for the intact presenile subjects (characteristic of the 5-year-old level); to 0.83 with only 10 per cent correct responses for medium presenile subjects; and to 0.92 with 4 per cent correct responses for deteriorated subjects (not considered effective for children of any age). Typical responses are shown in Figures 2 and 3.

Normal elderly subjects, though not achieving a completely accurate response, can make a creditable showing in this test, whereas intact presenile subjects cannot. Thus we consider that this test makes possible a differential diagnosis between normal and intact presenile subjects. Failure to make a substantially successful response to this test appears to indicate that the subject is presenile at best.

Lowenfeld Mosaic test. Developmental study of the child's response to the Mosaic test has shown (6) that, as the subject matures the responses "improve" from non-representational products without pattern, through non-representational products *with* pattern, to representational objects and scenes. The present study indicates that, with increasing deterioration, elderly subjects reverse this order in their responses to the Mosaic test.

As Table 6 shows, in normal elderly subjects the majority of responses were in the form of representational products, or fell in Class C. Intact presenile subjects made 17 per cent representational objects and 62 per cent non-representational designs with pattern. Of the medium presenile subjects only 7 per cent of the products were representational objects, 46 per cent non-representational designs

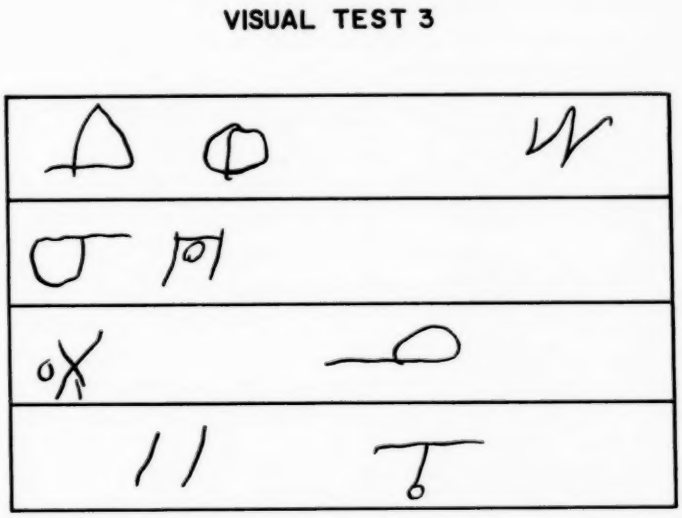

FIG. 2. Visual Test III as performed by 89-year-old woman (Mrs. M.R.). The results were regarded as at least 50 per cent satisfactory and thus were considered normal. Her severe agitation and anxiety, many complaints, and feelings of insecurity which were present on admission to the hospital disappeared when her constipation and other sources of mental strain were eliminated. Results with Visual Test III showed that no definite mental deterioration had taken place and only daily nursing care was required; therefore she was moved to the Home section. She has improved steadily, has social contact with other guests, and feels well. Without the test, permanent hospitalization might have been recommended.

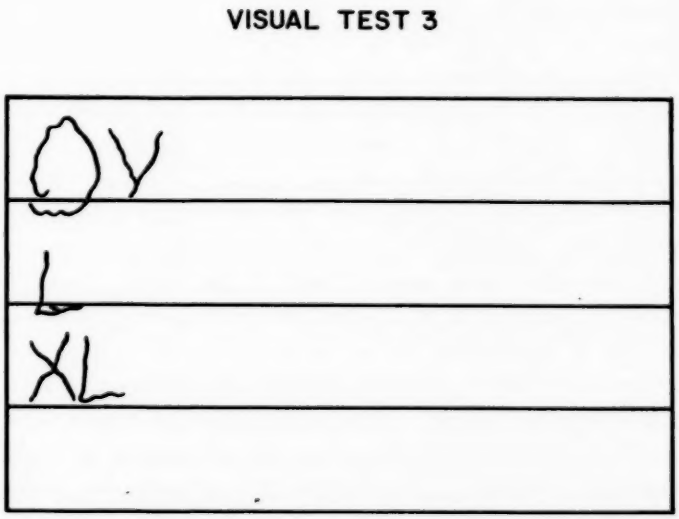

FIG. 3. Visual Test III as performed by Mrs. B.B., aged 83 years. The results indicate that even though all other tests might not reveal an impending breakdown, this woman would soon be unable to live by herself or in an Old Age Home, and would require closer supervision and care.

TABLE 6

Lowenfeld Mosaic Test: Percentage of Products Falling in Various Structural Categories

	Normal (7 Subjects)	Intact Presenile (24 Subjects)	Medium Presenile (16 Subjects)	Deteriorated (13 Subjects)
Refusals	14%	0%	7%	8%
All. just drop or pile		0%	13%	15%
A 2. scatter singly		4%	0%	15%
A 3. prefundamental		12%	13%	23%
A 4. "over-all"		4%	13%	0%
All A, or non-representational without pattern		20%	40%	53%
B 1. fundamental		8%	20%	23%
B 2. central design	28%	54%	26%	15%
All B, or non-representational with pattern	28%	62%	46%	38%
C 1. objects (representational)	57%	17%	7%	0%
All C, or representational	57%	17%	7%	0%
Success	71%	50%	40%	15%
Failure	29%	50%	60%	85%

with pattern, and 40 per cent non-representational designs without pattern. In deteriorated subjects, non-representational designs without pattern clearly predominated (53 per cent).

Furthermore, 71 per cent of the products of normal subjects could be considered "successful"; the corresponding proportion was 50 per cent for intact presenile subjects, 40 per cent for medium presenile subjects and only 15 per cent for the deteriorated subjects.

Thus the Mosaic test appears to be one of the most discriminative tests for determining the level of performance by elderly subjects. Any response which must be classified as "non-representational without pattern" indicates that subject is presenile or below. Any successful construction of even the simplest object suggests intact presenility or better.

Wechsler Intelligence Scale for Children. The following tests from the verbal scale of the WISC were given to all subjects: vocabulary, information, comprehension, arithmetic, similarities, digits (Table 7). Responses were scored in the standard manner for computing the so-called "raw score." Scaled score figures were obtained from WISC tables for subjects $15\frac{8}{12}$ to $15\frac{11}{12}$ years of age, the highest age level covered by the test. However, no effort was made to compute intelligence scores, since all subjects were obviously well beyond this age level.

Although the values obtained were not useful in computing intelligence quotients, when they were simply used as figures they gave a clear indication of the manner in which impairment of the responses paralleled deterioration of the subjects. Without exception, for both raw and scaled scores as well as for the total scale, the responses decreased in adequacy and accuracy with increasing deterioration of the subjects.

TABLE 7

Raw and Scaled Scores on Wechsler Intelligence Scale for Children (WISC)

	Normal (7 Subjects)	Intact Presenile (24 Subjects)	Medium Presenile (16 Subjects)	Deteriorated (143 Subjects)
Total Scale				
scaled score	66.75	41.95	29.33	17.31
Vocabulary				
raw score	67.14	46.83	40.25	16.38
scaled score	17.14	9.79	7.87	2.23
Information				
raw score	25.62	18.88	14.83	10.96
scaled score	16.25	9.55	6.66	4.80
Comprehension				
raw score	18.25	15.45	11.33	9.07
scaled score	11.50	8.59	6.33	4.31
Arithmetic				
raw score	12.25	10.27	8.33	5.46
scaled score	10.00	7.45	5.33	3.31
Similarities				
raw score	11.50	8.54	6.53	5.77
scaled score	10.75	5.67	4.00	3.92
Digits				
raw score	11.50	9.00	8.14	5.07
scaled score	10.75	7.50	6.21	3.23

Noteworthy was the relative degree of excellence in the various sub-tests. Among normal subjects, responses to both vocabulary and information sub-tests rated considerably higher (scaled score) than did responses to other sub-tests. Intact presenile subjects, also, made a somewhat better score on these two tests than on others. Even in the medium presenile group, the rating was somewhat higher on the vocabulary than on the other tests. Deteriorated subjects made their best scores on information and comprehension. Similarities rated lowest for all groups except the normal subjects, and even then, it was one of their lowest scores.

Table 7 shows approximately where, according to our findings, any given level of response to the WISC scored with regard to intactness or deterioration of performance. However, the WISC appeared to be less useful than other tests in the present series for determining levels of performance in elderly subjects.

Developmental level of responses to various tests

A study of Table 8, which indicates the corresponding ages in children at which responses of our subjects to the various tests could be rated, reveals one of the most difficult problems in the care and treatment of elderly persons, that is, the unevenness of response from one situation to another. Presumably normal subjects responded to some aspects of certain tests as poorly as a 4-year-old child, but to other aspects, as well as a 10-year-old child. In intact presenile subjects, the responses resembled those of children from 3 to 7 years of age; in the medium

TABLE 8

Developmental Level of Responses to Each Test for Each Group

Test	Normal (7 Subjects) (Mean Age, 76.28 yrs.)	Intact Presenile (24 Subjects) (Mean Age, 80.46 yrs)	Medium Presenile (16 Subjects) (Mean Age, 80.25 yrs.)	Deteriorated (13 Subjects) (Mean Age, 83.46 yrs.)
Rorschach	15N (6 yrs.) 1.85M: 1.14sC (10 yrs.) 64% F/85% F+ (8 yrs.) 4.4 content categories (4½ yrs.)	13N (3½ yrs.) 1.37M: 56sC (7 yrs.) 58% F/85% F+ (7 yrs.) 3.6 content categories (3 yrs.)	11N (2½ yrs.) 0.94M: 72sC (6 yrs.) 64% F/80% F+ (5½ yrs.) 3.6 content categories (3 yrs.)	7N (2 yrs.) 0.46M: 46sC (7 yrs.) 76% F/60% F+ (3 yrs.) 1.9 content categories (2 yrs.)
Gesell Cubes	tower bridge gate steps	tower bridge (5 yrs.) gate steps	tower bridge (4 yrs.) gate	tower (3 yrs.)
Gesell Copy Forms	circle cross square (6 yrs.+) triangle rectangle diamond	circle cross square (6 yrs.+) triangle rectangle diamond	circle cross square triangle rectangle diamond	circle cross square (5 yrs.) triangle
Monroe Visual I	all (5 yrs.+)	10.96 (5 yrs.)	10.20 (5 yrs.−)	4.69
Monroe Visual III	8.93 (8–9 yrs.)	2.77 (5 yrs.−)	0.83 (unscorable)	0.92 (unscorable)
Gesell Incomplete Man	8.57 parts (6 yrs.): arm, finger, leg, *foot*	7.87 parts (4½ yrs.): arm, finger, leg, hair, *eyes*, ear, neck	6.31 parts (4 yrs.): arm, *finger*, leg, hair, ears, neck	3.39 pts. (3 yrs.): leg, arm and one other
Lowenfeld Mosaic	patterned designs; objects (6 yrs.+)	patterned designs (5 yrs.)	non-patterned designs; patterned designs (4 yrs.)	non-patterned designs (3 yrs.)
WISC (score)	10–17	5–9	4–7	2–5
Range of behavior (ages)*	4½–10 yrs.	3–7 yrs.	2½–6 yrs.	2–5 yrs.

* Omitting the WISC, which yields no developmental or age designation.

presenile group, those of children from 2½ to 6 years of age; and in the deteriorated subjects, those of children from 2 to 5 years of age.

In spite of this, there was a pattern to the total response, in that for each individual test, the mean developmental age corresponding to the response decreased steadily with increasing deterioration of the subject. For example, the intact presenile subjects, as a group, performed less effectively than did the normal group, regardless of the unevenness of performance in any given subject at any time.

Differential diagnosis

Our findings indicate clearcut differences between groups of elderly subjects with different degrees of psychologic intactness, as tested with the present series of tests, as follows:

Normal elderly subjects responded to all these tests approximately as would normal adults of any age. They were successful in all cube, copy form, and visual tests as well as in making adequate responses to the Incomplete Man, Mosaic and WISC tests.

Intact presenile elderly subjects responded nearly as well, especially to the cube and copy form tests. They tended to leave out the foot on the Incomplete Man, but otherwise the response to this test was good. There were occasional errors in the Visual I test. In the Mosaic test they were less likely to depict objects and possibly to make non-representational designs without pattern. However, the significant clue which distinguished the normal from the intact presenile subjects was the fact that the latter could make only the most limited response to Visual III, whereas the normal persons responded adequately.

Medium presenile subjects responded adequately to all copy form tests and made only an occasional error in the Visual I test. However, they failed in the 10-cube steps, were unable to respond adequately to Visual III, added neither eyes nor foot to the Incomplete Man, and were far more likely to make non-representational designs without pattern than recognizable objects in the Mosaic test.

Deteriorated subjects. Deterioration was shown clearly with the present series of preschool and school-age tests. This group could build a tower of 10 cubes, but failed to build the bridge, gate and steps. They could copy correctly a circle, cross, square and triangle, but not the rectangle with diagonals or the diamond. They failed to a marked degree in both Visual I and Visual III tests and made only a meager response to the Incomplete Man test, usually adding only a leg, arm and one other part. In the Lowenfeld Mosaic test they were most likely to make non-representational designs without pattern.

Comment. As in other situations, final judgment as to the degree of intactness of function in any individual is ideally based upon the response of a series of tests rather than upon his response to a single test. However, with only 2 exceptions, in our present group of 60 subjects the classification of intactness of performance based on the Rorschach response alone was confirmed by the responses to subsequent tests.

* Omitting the WISC, which yields no developmental or age designation.

Age and sex

As various investigators have commented, and as one of our own earlier studies has shown (7), it is important in any study of behavior of elderly subjects to free oneself from over-concern with chronologic age. This is because the degree of intactness of performance seems in many instances surprisingly unrelated to age in years. Table 3 shows that females as old as 81 years of age may be found in the "normal" group, and females as young as 77 in the deteriorated group; or men as old as 89 in the intact presenile group, and men as young as 78 in the deteriorated group. Nevertheless, there is a conspicuous tendency, especially in the women, for the mean age of each group of subjects to increase with increasing deterioration of function (Table 3).

In this study the male and female groups were not sufficiently well matched for valid comparison, so we did not analyze the data separately for the two sexes.

COMMENT

This study was an attempt to determine the levels of intactness of personality and performance in a group of elderly subjects on the basis of their performance in a series of psychologic tests used customarily at the preschool and early school-age levels. From a practical point of view, currently available testing techniques have not furnished diagnostic data which give a satisfactory indication of what can actually be expected of elderly persons.

The hypothesis is offered, and apparently confirmed, that in spite of seeming intactness of function (good vocabulary, reasonably good memory, apparent social adequacy) many elderly persons are functioning, at least in some respects, at approximately a preschool level. For this reason, preschool and early school-age tests may yield a better index of the exact level of performance and possible function than will the type of adult intelligence and performance test usually administered.

It is further suggested that in order to measure adequately the decreasing levels of effective performance in elderly subjects, the clinician needs to understand the succeeding steps in the breakdown of any given function; these may prove to be in reverse order to the development of that function in childhood.

As Table 8 shows, there is a definite difference between normal and presenile subjects with regard to the Visual III test. The table also shows that easier and more reliable tests than the Rorschach may be utilized; thus time can be saved, and medical personnel can administer the tests instead of psychologists. In view of the large number of old persons needing evaluation, the time factor is of utmost importance. The application of these tests can help greatly in the care and placement of geriatric patients.

At present, on a trial basis, our supervisory registered nurses are administering the Visual III test to our total hospital population. We learned by this practical application to understand our patients better and to place them where the demands of daily living are not too great for their ability. If only verbalization tests were used, great injustice would be done to these persons who appear so intelligent but are lost when they have to exercise judgment without falling

back on old memories and experiences to guide them. This can be readily understood in evaluating the results of the Visual III test.

If an old person in a Home is not capable of keeping up with the others, he feels rejected. That brings on more confusion and excitement and starts him off on the downward path to total confusion. We cannot stress enough how important it is to evaluate the geriatric population exactly, and how helpful this can be in understanding these old people and in giving them better care. If a nurse sees that a patient doesn't keep himself clean, yet can talk very intelligently about politics or philosophy, she naturally thinks he is just mean—especially if he wets his clothing. By giving such an old person some simple psychologic tests, it can be demonstrated to the nursing personnel that he has insufficient judgment or insight in spite of his ability to talk so intelligently.

Only practical experience reveals how much can be done to keep these old people functioning on a certain level of mental ability instead of hastening their breakdown by asking too much of them. The results of these tests emphasize that old people are lost when they cannot utilize old experiences and memories. We all know of the mother-in-law who doesn't fit into the household because the members of the younger generation think she is unreasonable. She can be so nice to her guests, entertain so graciously, and talk so intelligently, but when she is alone she will do everything to make it miserable for the daughter-in-law. The main reason (perhaps in addition to the resentment caused by her son's marriage) is that, in many decisions the older woman has to make, she cannot utilize old experiences as she can when playing cards or entertaining. Then the trouble starts. Those old memories are valuable and that is why the elderly always refer to the good old days; nothing present is good. How can it be, if they do not understand it; and how can they understand it without being able to judge the present intelligently? The Visual III test reveals the break in the ability to judge. It is not claimed that Visual III is the ideal test, but it is useful in the process of developing a test which is more appropriate for our age groups. Any help is valuable. The first impression is that Visual III is a difficult test, but if we are satisfied with 50 per cent efficiency (as we are), it becomes quite easy. When a patient can reproduce 2 out of 4 figures on each card, we regard him as normal. A good way to start is to tell the patients that this is a test to help us appraise their vision; then they become very cooperative.

Many old people use lifetime experiences so well that we speak of the wisdom of old age, but in others cerebral changes take place that affect their mentality. Preschool psychologic tests show that they are functioning on a very low level in areas where they cannot use their previous experiences.

SUMMARY

Sixty subjects were chosen from an initial group of 100 guests and patients of the Masonic Home and Hospital in Wallingford, Connecticut, who had each been given a Rorschach test. These 60 subjects underwent further examination with 7 additional psychologic tests. The findings appear to confirm the hypothesis that preschool and school-age tests permit adequate differential diagnosis be-

tween groups of adult normal, intact presenile, medium presenile, and deteriorated subjects. The Visual III test is especially helpful. The degree of intactness of function appears to be largely independent of the chronologic age of subjects.

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DEPRESSION—ITS TREATMENT WITH ETRYPTAMINE ACETATE

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This report concerns the clinical use of a new monamine oxidase inhibitor in the treatment of reactive and involutional depression. An indole, alpha-ethyltryptamine, it is designated by the generic name etryptamine acetate[1] and the trade name Monase®. In contrast to monamine oxidase inhibitors having the hydrazine configuration, etryptamine acetate *reversibly* inhibits monamine oxidase; thus previously blocked enzyme again becomes active unless more medication is taken within twenty-four to forty-eight hours (1, 2). Etryptamine acetate is less toxic than other monamine oxidase inhibitors: it has little hepatic, hematologic or renal toxicity and it causes no significant degree of orthostatic hypotension.

MATERIALS AND METHODS

Patients: Sixty-nine ambulatory patients were studied—31 men and 38 women. For the 24 noninstitutionalized patients, aged 46 to 66 years, the diagnosis was reactive or situational depression. For the remaining 45 patients, aged 61 to 93 years, the diagnosis was advanced involutional depression. The latter group lived in a well organized geriatric facility, where accurate, round-the-clock observation by trained personnel was available.

The 24 ambulatory patients with reactive depression were in acute or subacute depressive states triggered by recent events which were consciously or unconsciously intolerable. Consequently, these patients withdrew from their real life situations and became apathetic, afraid, tired and hypochondriacal.

The 45 patients with involutional depression had experienced symptoms of despondency, withdrawal, hypochondria, marked fatigue, apathy, pessimism, and self-debasement for two to twenty-three years. Some had occasional delusions and frequent episodes of anxiety, anorexia, and insomnia; they often manifested an inability to communicate. Most of them had functioned poorly on an interpersonal basis for a long time. Many had received prior antidepressive therapy—electric shock, iproniazid, nialamide, dextroamphetamine sulfate, or other drugs. Iproniazid partially controlled their depression, but was discontinued because of toxicity.

Drug: Etryptamine acetate (either 5 mg. or 3 mg.) and a placebo were available in identical-appearing, coated, compressed tablets. The placebo was used in a single-blind study with the 45 institutionalized patients after the initial response to etryptamine acetate had been determined in a nine-week period.

Dosage: At least two weeks prior to treatment, other psychopharmaceutical medications were discontinued. Initially, the patients with reactive depression received etryptamine acetate, 5 mg. three times daily. If this dosage proved ineffective after three weeks of therapy, 5-mg. increases in the total daily dose were made at intervals of seven days until a maximal daily dose of 30 mg. was reached or until a satisfactory response occurred. The older and more feeble patients with involutional depression received smaller amounts;

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[1] Etryptamine acetate was supplied as Monase by The Upjohn Company. This study was supported by a grant from The Upjohn Company.

the initial dosage was 3 to 5 mg. twice daily, and the maximal daily dose was 25 mg. The dose was increased in a manner corresponding to that used in treating the reactive group.

Five patients in good general health and free of cardiovascular disease had particularly resistant involutional depression. Their daily dose of etryptamine acetate was increased to 50 mg. for three to four weeks in order to determine whether massive doses could overcome long-standing involutional depression.

Grading of results: Evaluation of the results of therapy was based largely on subjective improvement. The only measured objective change was weight gain; this verified subjective improvement in appetite. A "poor" rating indicated no benefit after four weeks of continuous therapy with 25 to 30 mg. of etryptamine acetate daily to elicit improvement in depression. A "moderate" rating indicated a response characterized by increased energy, brighter mood, and improved interpersonal communication, with some elements of depression remaining. A "good" rating indicated a response characterized by increased energy and a return to pre-illness ability to handle interpersonal relations without frequent relapses into a state of depression.

RESULTS

Table 1 is a summary of the results of treatment with etryptamine acetate 25 to 30 mg. daily. Sixteen (67 per cent) of 24 patients with reactive depression responded satisfactorily, whereas only 21 (47 per cent) of 45 patients with involutional depression responded. Good results were obtained in 46 per cent of the reactive group and 13 per cent of the involutional group, emphasizing the difference in responsiveness.

Weight gains attributed to improved appetite secondary to treatment were as follows: 12 (50 per cent) of the patients in the reactive group gained 2 to 5 pounds during the nine weeks of observation; 18 (40 per cent) of the patients in the involutional group gained 2 to 7 pounds in the same period.

The patients with involutional depression reacted to the placebo substitute for etryptamine acetate as indicated in Table 2. In only 4 of the 21 patients with good or moderate results did this rating continue; in the other 17 a relapse occurred.

Of the 5 patients with resistant involutional depression who were given 50 mg. of etryptamine acetate daily, 1 showed moderate clinical improvement. At this dosage level, a tranquilizer was added to the daily regimen of 3 of the 5 patients because of side-effects (palpitation and nervousness) attributed to the drug. The side-effects were well controlled by this means.

Toxicity. Repeated blood counts, urinalyses, and hepatic and renal function tests yielded normal findings in all patients. There was no evidence of toxicity or altered physiology.

Side-effects. Palpitation and nervousness occurred in 4 patients taking 30 mg. of etryptamine acetate daily and in 3 patients taking 50 mg. daily; these symptoms were readily controlled with ataraxics. Five elderly patients receiving 20 mg. daily had sensations of vertigo, but did not fall. Two patients with advanced arteriosclerotic heart disease had mild anginal pain when taking 20 mg. daily. Abdominal cramping and nausea occurred in 3 patients, but these symptoms were not attributable to the drug.

In no instance was there any evidence of hypotension or disturbance of the usual sleep pattern.

TABLE 1

Results of Treatment of Depression With Maximal Doses of Etryptamine Acetate*

Type of Depression	No. of Patients	Results		
		Good	Moderate	Poor
Reactive	24	11 (46%)	5 (21%)	8 (33%)
Involutional	45	6 (13%)	15 (33%)	24 (53%)
Totals	69	17 (25%)	20 (29%)	32 (46%)

* 30 mg. daily in the reactive group; 25 mg. daily in the involutional group.

TABLE 2

Results of Treatment of Involutional Group (45 Patients) with Placebo After Effect of Etryptamine had been Determined

Good or Moderate Results Continued	Relapse After Good to Moderate Results	Depression Continued
4	17	24

DISCUSSION

The reversible action of etryptamine acetate in blocking monamine oxidase probably contributes to its safety, since there is little likelihood of cumulative overdosage. Recovery from the effects of a single dose is independent of the patient's ability to synthesize new monamine oxidase. Orthostatic hypotension occurs only after one to three weeks of treatment with other monamine oxidase inhibitors (3); thus the reversibility of the action of etryptamine acetate may also account for the absence of this side-effect in the present study.

The difference in responsiveness between the reactive and involutional patients may have been related to the factors of habit and borderline senile psychosis that predominated in the latter group. However, a 47 per cent clinical response in patients who previously had remained depressed for two to twenty-three years should not be ignored—particularly in view of the small number of patients who continued to respond when, unknown to them, a placebo was substituted for the etryptamine acetate.

SUMMARY

Sixteen of 24 patients with reactive depression experienced "good" or "moderate" improvement when treated with etryptamine acetate, 30 mg. daily. Twenty-one of 45 patients with involutional depression responded similarly to 25 mg. daily. A relapse occurred in 17 of these 21 previously improved patients following placebo substitution (single-blind study). No patient responded to the placebo who had not responded to the active drug.

No serious side-effects were observed, nor any evidence of drug toxicity. The reversibility of the inhibition of monamine oxidase by etryptamine acetate may

partially account for the relative safety of this drug, and particularly the absence of hypotension as a side-effect.

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HOST-TUMOR ANTAGONISM. XIX. CANCER AND DYSFUNCTION OF THE LIVER*

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STATEMENT OF THE PROBLEM

Many authorities have adduced evidence for the possibility of liver dysfunction in patients with cancer, and in experimental animals with transplanted cancer. Thus it has been known for a long time that the presence of a cancer anywhere in the body puts a strain on the liver.

Recently, a book was published by the English surgeon, Kaspar Blond (1), whose central theme is that cancer is caused by certain toxins in the blood stream (and therefore also in certain organs), which are present only because they cannot be detoxified by a damaged liver. If the liver were not damaged, the toxins would be destroyed and no cancer would result. On this basis the prevention and treatment of cancer would be simple, at least theoretically, even if it did not prove to be so simple in actuality. This theoretical concept seems of such importance, however, that it was thought worth while to examine again the basis for the reports of liver dysfunction in cancer patients and in cancer-bearing animals.

EVIDENCE FOR LIVER DYSFUNCTION IN EXPERIMENTAL ANIMALS WITH TRANSPLANTED TUMORS

Greenstein (2), in normal and cancerous animals, investigated under the same conditions a number of chemical and enzymatic systems in tissues which were located at a distance from the tumor. None of these animals had metastases and they were in a good nutritional state. Greenstein was surprised to find that nearly all enzyme systems in the tissues studied were at nearly the same level in normal and in cancer-bearing animals. There was only one enzyme system, catalase, and only in the liver, which was markedly affected by the presence of a cancer elsewhere in the body. Some suggestion of this phenomenon had already been reported years earlier by Brahn (3).

Catalase is a hematoporphyrin enzyme that acts on hydrogen peroxide and decomposes it to water and oxygen. When liver homogenates, prepared under identical conditions from normal and cancer-bearing animals were compared, the rate of evolution of oxygen from added hydrogen peroxide was always less in cancer-bearing animals. There always was less catalase activity per unit of nitrogen of tissue in the livers of cancer-bearing animals. Other enzyme systems such as cytochrome C, cytochrome oxidase, or acid and alkaline phosphatase, were always at normal levels in the same livers of cancer-bearing animals which simultaneously showed the marked decrease in catalase levels (2).

* Parts I–XVIII of this study were published in the July, August, November (1956), April, May, June, August, October, November (1957), May, July (1958), May, September (1959), May, July (1960), and January and July (1961) issues of this Journal.

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The reduction of the liver catalase level was observed only in animals bearing rapidly growing tumors. An interesting series of experiments was carried out to show the reversibility of liver catalase activity.

Rats inoculated subcutaneously with a rapidly growing transplanted tumor demonstrated a proportionate decrease in the liver catalase level with growth of the tumor. When the tumor was surgically removed, catalase activity was restored to normal in forty-eight hours. When the rats were re-inoculated with tumor, the hepatic catalase level was again depressed. Mice inoculated in the tail with a rapidly growing tumor showed a decrease in liver catalase activity, which returned to normal after caudectomy. Pregnant mice near term showed normal catalase activity. Therefore the effect on liver catalase is not due to growing tissue per se, but to a growing tissue which is of a special type—a cancer. The effect is noted only in the living animal; homogenates of cancer tissue when mixed with homogenates of liver in a test tube have no influence on the catalase activity of each tissue (2).

Other authorities (4–6) besides Greenstein found that liver catalase levels were reduced in cancer-bearing animals. Begg (4) noted that, besides the lowered hepatic catalase activity in cancerous animals, there was also an enlargement of the adrenal glands with loss of ascorbic acid and cholesterol.

Greenstein thought it possible that the lowering of catalase activity is due to some toxic material elaborated by the tumor which, by passage through the circulation, affects the synthesis or storage of catalase in the liver. Nakahara and Fukuoka (7) reported the isolation from human cancers of a proteose-like material that caused a marked reduction of liver catalase when injected intraperitoneally into mice. This "toxohormone" was later demonstrated in mouse tumors also (8). It was found that the "toxohormone" effect could be neutralized by the injection of iron salts. Therefore it appeared probable this substance combined with the iron in the circulation and in the iron stores, and thus limited the synthesis of iron-containing catalase molecules (9).

Bucher and Glinos (10) studied the distribution of phosphatase in rat liver during regeneration and after administration of p-dimethylaminoazobenzene. An increase in phosphatase activity was demonstrated in various plants and animal tissues during periods of rapid growth. The hyperplastic and regenerative changes that appear in rat liver following the administration of the carcinogen, p-dimethylaminoazobenzene, may be regarded as a special instance of growth activity.

Bucher and Glinos studied the histologic distribution of alkaline phosphatase in rat liver during the transition from a normal to a neoplastic state, to see whether any particular pattern of changes precedes the formation of hepatoma. Their findings indicate that during regeneration and during certain phases of the proliferative process following administration of p-dimethylaminoazobenzene, the phosphatase is increased.

Orr (11) noted the effect of butter yellow (p-dimethylaminoazobenzene) on the histology of the rat's liver during the course of carcinogenesis. Butter yellow was added to the food of 200 white rats, and the course of the histologic changes in the liver was followed. The usual sequence was proliferation of connective

tissue cells in the portal systems; extension of granulation tissue from the latter into the parenchyma, with degeneration of the contiguous liver cells; atypical regenerative proliferation of the bile-duct and liver epithelium, leading ultimately to non-architectural nodular hyperplasia; and finally a macroscopically hob-nailed liver in which there was a certain incidence of tumor development. Administration of butter yellow was stopped after two hundred and thirty-two days. In two or three months the liver returned to normal, except for the presence of tumors. It was shown that cancer could arise while the cirrhosis was still in the reversible phase.

Orr believed that the primary effect of butter yellow on the liver parenchyma is destruction and that the proliferative changes are in the nature of regeneration.

Chan, McDonald and Cole (12) investigated the influence of liver damage on the development of Walker-256 carcinosarcoma. White rats were first given injections of carbon tetrachloride subcutaneously to produce acute liver damage, and then were given injections of Walker-256 cell suspensions either subcutaneously or intraportally. Suitable controls received injections of the Walker-256 cells only. In the group receiving intraportal injections, 42 per cent of the animals with hepatic damage also had tumors, as against 18 per cent in the control group. In the group given subcutaneous injections, 50 per cent of the animals with liver damage also had tumors, as against 20 per cent in the control group.

The authors felt that the regenerative power of the liver acutely damaged by carbon tetrachloride was the important factor in increasing the incidence of tumor development.

PRODUCTION OF TUMORS IN ANIMALS BY INDUCING CHRONIC CHOLINE DEFICIENCY

Copeland and Salmon (13) induced chronic choline deficiency in the rat with a choline-deficient diet supplemented by minimal doses of choline to prevent death from acute choline deficiency. Of the 88 rats studied, 50 survived for eight to sixteen months with a choline-deficient diet.

Sections from the livers of rats that had received the choline-deficient diet for three months showed a peculiar zonal distribution of fatty infiltration and degeneration, which was thought to be a pre-cirrhotic stage. There was beginning evidence of a rapid rate of cell destruction and cell regeneration. Severe hepatic cirrhosis developed in all rats that received the choline-deficient diet for eight months or longer. The livers of 50 per cent of the animals receiving the choline-deficient diet contained cysts, which appeared to be groups of dilated sinusoids. There was a focal loss of parenchymal cells, with a proliferation of endothelial cells in these areas. In some lobes of the liver numerous mitotic figures were found. Hepatoma-like neoplasms developed in 10 per cent of the livers, and adenocarcinomas in 30 per cent. Primary carcinoma of the lungs occurred in 38 per cent of the rats, subcutaneous and peritoneal hemangio-epitheliomas in 10 per cent, and retroperitoneal sarcomas in 6 per cent.

Thus neoplasms of one or several types were observed in 58 per cent of the choline-deficient animals. No similar lesions were found in litter-mate controls receiving the same diet supplemented with 20 mg. of choline per rat daily.

This was interpreted as meaning that the marked accumulation of fat in the liver cells resulting from choline deficiency initiated a sequence of responses which resulted in profound changes in the structure and behavior of the cells. Cell degeneration and cell regeneration were greatly stimulated; connective tissue cells replaced normal liver cells; extensive bile-duct proliferation, severe hyperplasia and exaggerated mitosis occurred; and eventually neoplastic cells appeared.

In a more recent study of chronic choline deficiency, Salmon and Copeland (14) found pulmonary metastases from liver tumors in 2 rats. In another experiment using the choline-deficient diet in chickens, the results were similar to those in rats. Fatty changes and cirrhosis of the liver were common. Hepatic lesions considered to be malignant developed in 12 cases, and "atypical regeneration nodules" in 11 other cases. Definite hemochromatosis (hepatic cirrhosis with iron deposits in the liver and other organs) developed in 25 per cent of the choline-deficient chickens, and elevated quantities of iron-positive pigments were found in the liver and kidneys of all the chickens. In the choline-deficient rats, a smaller amount of iron-positive pigment was found, but even in these animals it was much greater than in the controls. The choline-deficient diets were also deficient in vitamin B_{12}, a vitamin with a definite choline-sparing action.

In similarly designed studies, hepatomas have been produced in mice fed a complete semi-synthetic diet mixed with an equal amount of bentonite by weight (15). Bentonite is a cation-exchange silicate that apparently removes choline from the contents of the digestive tract so that it cannot be absorbed into the body, thus resulting in a deficiency.

POSSIBLE RELATIONSHIP BETWEEN ARGININE AND CHOLINE IN CANCER

Several authors (16) have reported a high arginine content in neoplastic tissue, as well as in regenerating and fetal tissues. Vrat (16d), in addition, found that the blood has a high arginine content in these states, especially in cases of carcinoma. Vrat's findings seem extremely significant. His results fit in well with our own concepts, based on work conducted with methods entirely different from his (17). We found that in patients with cirrhosis of the liver and in cases of gastro-intestinal and some other carcinomas, if a large test dose of choline is given, it is not utilized but is excreted in the urine. The same test dose of choline given to a normal subject is not excreted in the urine, but is utilized presumably in the formation of phospholipid. Wastage of choline is probably associated with choline deficiency (18). Our studies indicate that the choline excretion which occurs in cases of choline deficiency probably is due to inability of the patient to utilize the choline to form phospholipid.

Arginine and choline have one link in common. They are both utilized by the body to form creatine, according to the reactions (19):

I.
$$\underset{\text{(Arginine)}}{NH_2C(NH)\cdot NH\cdot (CH_2)_3CHNH_2\cdot COOH} + \underset{\text{(Glycine)}}{NH_2\cdot CH_2\cdot COOH} \xrightarrow{\text{(Kidney)}} \underset{\text{(Guanidoacetic Acid)}}{NH_2\cdot C(NH)\cdot NH\cdot CH_2COOH}$$

$$NH_2 \cdot C(NH) \cdot NH \cdot CH_2 \cdot COOH + (\text{Methyl groups}^*)$$
(Guanidoacetic Acid)

II.
$$\xrightarrow{\text{(Liver)}} NH_2 \cdot C(NH) \cdot N(CH_3) \cdot CH_2 \cdot COOH$$
(Creatine)

The first reaction takes place in the kidney and the second takes place in the liver.

In the livers of patients with cirrhosis, methylation is impaired, and guanidoacetic acid piles up in the blood and finally is excreted into the urine. Probably this also occurs in carcinoma patients, but it has not been proved.

If, in patients with carcinoma, the methyl groups available for the methylation of guanidoacetic acid are insufficient, reaction No. I may pile up and cause first an increase in guanidoacetic acid and finally an increase in arginine. Presumably this would result in a high blood arginine content in the patient with cancer. This significant point was discussed by Vrat.

Vrat (20) also noted that there was a decrease in arginase activity in neoplastic diseases. Arginase is formed in the liver and catalyzes the hydrolysis of arginine to form ornithine and urea. Vrat showed that arginase injected into mice bearing spontaneous adenocarcinomas of the breast, caused a reduction in the size of the neoplasm and considerable alteration in the histologic appearance of the cancer cell. Cytochemical tests demonstrated that the tumor contained no arginine, but rather, urea. Vrat (21) also noted a similar effect of arginase on the growth of transplanted mammary carcinoma in C_3H mice.

As noted in detail in a previous section, Copeland and Salmon (13) noted the development of various tumors in the cirrhotic livers of choline-deficient rats. Perhaps the arginine-arginase equilibrium was disturbed in their rats, as suggested by the work of Vrat. Choline deficiency would not allow for the completion of reaction No. II, but since reaction No. I would be unchecked, it would presumably result in a piling up of guanidoacetic acid and arginine in the tissues and blood. In this manner, arginine excess and choline deficiency can be rationalized as separate phases of the same process. Taken in conjunction with our own work on choline excretion in cases of gastro-intestinal cancer (17), it would seem that this small area is a fruitful field for intensive and concerted research.

ENHANCEMENT BY CHOLINE OF THE FUNCTION OF THE RETICULO-ENDOTHELIAL SYSTEM: APPLICATION TO THE ADJUVANT TREATMENT OF MALIGNANCY

Various methods, including whole body irradiation (22) and cortisone (23), have been used to depress the reticulo-endothelial system (RES). Some substances, such as Trypan blue, apparently damage the RES and then produce a hyperfunctional state (24). It is claimed that various other substances, such as antireticular cytotoxic serum (ACS) and histamine, stimulate the RES; however, the practical value of ACS in this respect remains in doubt. It has also been reported that choline causes hyperfunction of the RES (25).

Chevremont (26, 27) found that choline stimulated histiocyte formation in tissue cultures. Heller (25) used the rate of phagocytosis of radioactive chromium

phosphate as a test of function, and demonstrated that choline caused a 100 per cent increase in RES function compared to the condition in controls treated with saline. Heller (23) further showed that the RES-depressing effect of 0.25 mg. of cortisone could be completely abolished by administration of an adequate amount of choline.

Under these circumstances, it was of great interest that several German investigators claimed that choline was of benefit in the treatment of carcinoma, either alone, or as an adjuvant to radiation therapy. However, these authors had a distinctly different rationale for the use of choline in cancer therapy.

Fecht (28) was of the opinion that in vagotonic persons carcinoma rarely develops, and if it does, it is usually not highly malignant. Conversely, sympatheticotonic persons are particularly prone to cancer. He stated that it was possible to inhibit the local growth of carcinoma by cutting the afferent sympathetic nerve fibers. He attributed the favorable effect of roentgen-rays partly to stimulation of the vagus nerve, and thought that increased vagal tone enhanced the effect of insulin, thereby lowering the level of blood sugar and thus the nutrition of the tumor. According to Fecht, choline produces inflammatory reactions in the carcinomatous lesion, and this inflammation stimulates rather than prevents healing, since it increases local resistance. Moreover, a cholesterin-rich diet may be one cause for the increasing incidence of carcinoma, as cholesterol apparently suppresses vagal activity and supports sympathetic activity. Choline counteracts this effect of cholesterol, in his view.

Fecht found that in animal experiments, neostigmine (Prostigmin)—which is an even more intensive vagal stimulating substance—had an effect similar to that of choline, namely, inhibition or complete destruction of the carcinoma. Following pretreatment with choline or neostigmine, the carcinoma implants failed to grow in 70 per cent of the animals. Fecht stated that in man the results of treatment of carcinoma carried out on the basis of these findings were in agreement with the results in animals.

Becker (29) found that choline therapy combined with irradiation produced considerable improvement in hopelessly ill patients. Becker gave his patients 2 to 10 Gm. of choline daily, at the rate of 0.5 or 1.0 Gm. every one or two hours during the day. The tumors appeared to be inhibited in growth, but did not disappear. Improvement was noted in 25 per cent of 80 severely ill patients.

Velten (30) stated that there was a definite change in the character of the growth of tumors in patients who had been treated with choline. When the drug first took effect there was a marked inflammatory cellular reaction, which was followed in the course of choline therapy by the gradual devitalization of the tumor cells. Finally, after prolonged treatment, connective tissue had replaced the tumor tissue. The condition necessary for effective treatment appeared to be long-continued high dosage.

The findings in human tumors have been confined to several studies of solid mouse tumors. According to a report (Lettre (31)) quoted by Velten, the effect of choline on mouse-ascites tumor consisted of an increase in giant cells in the metaphase, with inhibition of division of cytoplasm in the anaphase.

Gansslen (32) believed that the therapeutic effect of choline is one of physiologic inhibition of growth and that there is no specific effect on tumor cells. In mature cells this results in a life-prolonging, protective effect. In cancer cells it was found that choline inhibits the dissolution of the cellular nuclear membrane and leads to the formation of giant cells.

These unstable giant cells are rapidly destroyed and prevent further cell proliferation. Gansslen found that sulfonamides acted also in this manner on cancer cells, so he combined sulfonamides and choline as a suitable form of basic treatment in tumor control. Over a period of years, this author claims to have treated more than 100 inoperable tumors with choline. He stated that although the results were variable, they were beneficial in many cases.

Kraus (33) thought that choline might inhibit the growth of immature cancer cells. He administered choline citrate to carcinoma patients orally, in a total daily dosage of about 1.75 Gm. of choline. In some instances, a decrease in the size of the tumors was noted. Kraus recommended that choline medication be continued for a long time.

Becker (34) in another study, used choline for the treatment of tumors that were not suitable for treatment with surgery or radiation. He used choline chlorate (5 to 25 per cent solution) in a daily dosage of 5 to 15 Gm., depending upon the condition of the patient and the reaction of the tumor. The choline was administered by intravenous or intrasternal drip infusion; when this was impossible, it was given by intragastric or rectal drip. The patient's general condition improved after the first few infusions, associated with increased appetite and a slow gain in weight.

The most impressive finding was the definite affinity of choline for the tumor. There was a definite local reaction consisting of pain, redness and swelling in the region of the tumor and the metastatic nodules. For the first few days the tumor became smaller and harder. Lymph-node metastases were influenced more rapidly than the primary tumor. In some patients the ascites disappeared and did not recur. Necrosis was rare in the tumor region.

The first perceptible histologic changes occurred after about 60 to 80 Gm. of choline had been given. The tumor became more sharply demarcated from the surrounding tissue. There was also proliferation of connective tissue. Collections of inflammatory cells, chiefly leukocytes, were seen in the immediate neighborhood of the tumor-cell complexes. Becker believed that the choline combined with the malignant cells and produced macroscopic and microscopic changes, and also acted indirectly on the vegetative nervous system.

Whatever the explanation offered by these German authors for the efficacy of choline as adjuvant therapy in human carcinoma, their reported results require attention. A controlled clinical trial is definitely indicated.

EVIDENCE FOR DYSFUNCTION OF THE LIVER IN PATIENTS WITH CANCER

Abels and his associates (35) demonstrated that about 85 per cent of patients with cancer of the gastro-intestinal tract had abnormally low plasma levels of vitamin A. In most of these patients the low levels were considered to be due to

an inability of the liver to store the vitamin or to distribute it properly. These investigators then surveyed liver function in other patients with carcinoma of the gastro-intestinal tract, by means of a series of tests which revealed hepatic abnormalities in the majority of the patients (36). Among these tests were: 1) loading with vitamin A and then the determination of the plasma vitamin A level; 2) loading with vitamin K and then the determination of the prothrombin time; 3) the level of the serum proteins and partition of the proteins; 4) the concentration of serum bilirubin; 5) the urinary excretion of glucuronates; 6) the mean corpuscular volume of the erythrocytes; 7) the urinary and fecal excretion of urobilinogen; and 8) the measurement of blood cholesterol and cholesterol esters. It is known that patients with liver insufficiency have a low prothrombin level that is not increased by giving vitamin K, that they have a low plasma level of vitamin A, that the increase in plasma bilirubin concentration parallels the inability of the liver to excrete the pigment, and that the plasma levels of total protein and albumen are low. Moreover, patients with liver disease and anemia may have macrocytosis provided the anemia is not due to blood loss; esterification of cholesterol is low, urinary excretion of glucuronates is decreased, and urinary excretion of urobilinogen is elevated though fecal excretion is normal.

Using these tests of hepatic function along with palpation for the detection of liver enlargement, Abels *et al.* (35, 36) came to the conclusion that among patients with cancer of the gastro-intestinal tract there is a very high incidence of hepatic dysfunction, and that following removal of the cancer the incidence of hepatic dysfunction drops. This observation would suggest that the presence of such a cancer results in a type of hepatic insufficiency that is largely reversible.

These investigators (37) also noted that the intravenous administration of glycine to normal subjects and to patients with benign gastro-intestinal disorders resulted in an increased urinary excretion of creatine and creatinine. The intravenous administration of comparable amounts of glycine to patients with gastro-intestinal cancer and hepatic cirrhosis failed to increase the urinary output of creatine and creatinine in the great majority of those tested. The simultaneous ingestion of choline, as a source of free methyl groups, failed to increase the creatine and creatinine excreted in the urine of patients with gastro-intestinal cancer or hepatic cirrhosis. The authors concluded that the failure of glycine to increase the output of creatine and creatinine in the urine of patients with gastro-intestinal cancer was due to a co-existing hepatic insufficiency.

On the other hand, Abels, Pack and Rhoads (38) noted that patients with gastro-intestinal cancer still had a normal capacity to esterify phenols, a hepatic function which was markedly decreased in patients with decompensated cirrhosis. From the data, it appeared that the impaired hepatic synthesis or conjugation of glucuronic acid in patients with gastro-intestinal cancer did not limit the capacity of the liver to conjugate phenols. It is possible that the detoxification of phenols in patients with cancer of the gastro-intestinal tract is not dependent on the synthesis of glucuronic acid. It may be inferred that hepatic damage from various causes may not affect precisely the same hepatic functions.

Kobayashi and co-workers (39) made a histochemical study of the liver in pa-

tients with cancer. A small specimen of the liver was removed at the time of laparotomy (for various indications) and submitted to histochemical investigation.

In patients with cancer, the liver acid and alkaline phosphatase levels were higher than in non-cancer patients. High phosphatase activity was often observed even in cases in which liver function tests yielded normal findings. The glycogen content of the liver in cancer patients was much lower than in patients without cancer.

Trieger *et al.* (40) stressed the significance of chronic hepatic disease as a predisposing factor in cancer of the tongue. They then turned their attention (41) to mouth cancer (which comprises about 5 per cent of all cancers), and found that the consumption of alcohol was heavy in 75 per cent of patients with cancer of the floor of the mouth, palate and tonsillar fossa. The incidence of overt hepatic cirrhosis was 58.8 per cent among 68 patients who were thoroughly evaluated when admitted to the Massachusetts General Hospital for treatment of mouth cancer. This figure does not represent the additional group of 84 cases of oral cancer for which adequate information was lacking in the hospital records.

The exact mode of action of alcohol in the development of oral cancer may be the local effect on the oral mucosa, but more likely it is secondary to a generalized change in the mucosal substrata due to malnutrition and resultant hepatic dysfunction. This theory is further reinforced by observations on the group of patients with non-alcoholic cirrhosis in whom mouth cancer developed. For mouth cancer associated with cirrhosis, the five-year survival rate was 19 per cent, whereas for mouth cancer alone the rate was 40.3 per cent. The average age at the time of diagnosis for patients with cancer of the mouth and hepatic cirrhosis was 57 years, whereas it was 70 years for the patients without cirrhosis. This study does not negate the importance of oral irritants as an exciting cause of cancer.

Patients with cirrhosis of the liver and carcinoma of the gastro-intestinal tract were found by the present author and his colleagues (17, 42) to have a similar defect in choline metabolism, in the sense that there was a measurable amount of choline in the urine after administration of a test dose. Castro-Mendoza and associates (43) had previously called attention to the experimental observation that the urine of normal persons or of normal dogs does not contain choline. They found that, in normal persons, a surcharge of choline does not produce an elimination of this substance. Experimental injury to the liver of dogs caused by administration of carbon tetrachloride gave rise to spontaneous cholinuria, and to marked cholinuria after surcharge. They stated that the same phenomenon occurred in patients with liver disease (cirrhosis, hepatitis). Furthermore, in such patients, the spontaneous cholinuria and the marked cholinuria after choline surcharge were due to poor utilization of choline by the liver with respect to the functions of fermentation, phospholipid formation and transmethylation.

The present author and his colleagues found that excretion of choline after a choline-loading test was the rule in cases of cirrhosis of the liver, but noted absence of urinary choline after choline loading in cases of hepatitis. There was

no excretion of choline after surcharge in normal people with our method of choline loading and our method of testing for choline excretion.

Other than in cases of cirrhosis of the liver, we found that excretion of choline after surcharge occurred most often in patients having carcinoma of the gastrointestinal tract, with or without hepatic metastases. These studies indicate that a similar pattern of liver dysfunction occurs in cirrhosis of the liver and in gastrointestinal malignancy.

Cayer and Cornatzer (18), using an isotopic technique, found that the administration of a large dose of choline to rats receiving a deficient diet, caused a marked stimulation of phospholipid turnover in the liver and plasma. This increased turnover was no longer obtained after an adequate diet was fed. The same phenomenon occurred in patients with cirrhosis of the liver. The patients were given an intramuscular injection of radiophosphorus and a large dose of lipotropic substance (choline or methionine), and the radioactivity of the plasma lipoid phosphorus was determined. After several months of treatment, the values were again determined. The amount of radioactive phosphorus in the plasma lipids was much higher in the early test than in the later tests. Although our measurements were not of this type, we also found constant changes that could possibly be equated with Cayer and Cornatzer's results. In a severe case of cirrhosis that had not been treated, we found a high urinary choline excretion; after this same patient was treated with lipotropic substances and diet, no choline could be detected in the urine. Thus we might say that a high choline excretion after surcharge (with our method of choline-loading) probably reflects a state of relative deficiency of lipotropic substances and a need for this form of treatment.

LIVER DYSFUNCTION IN THE GENESIS OF CANCER (BLOND'S THEORY)

Blond (1) theorized that cancer is the morphologic manifestation of a metabolic disorder of the liver—specifically, that cancer is a mutation of somatic tissues caused by a chronic damage to the liver. Moreover, the structural changes in the somatic tissues are the result, and not the cause of the liver damage.

According to Blond, inversion of the blood stream is one of the most striking symptoms of portal hypertension (which in turn is the result of liver damage). Crucial points in his theory are inversion of the blood stream (*e.g.*, portal blood being shunted to the digestive organs) in patients with liver damage, and the presence of nutritional toxins likewise due to the liver damage. Organs and structures that cannot be reached by inversion of the portal blood stream can be reached by known or unknown porto-caval shunts.

He states emphatically that the only cancer-provoking agent is the accumulation in the digestive organs of toxins (not destroyed because of liver damage) which are carried through porto-caval shunts to remote parts of the body, to traumatic scars, to skin and lip lesions, and to other hyperemic organs such as the lungs; without the presence of undetoxified nutritional toxins in the blood stream, cancer would never arise.

Blond's conclusions are unique and possibly far-reaching, they should be quoted exactly: "All hepatopathogenic agents provoking liver damage and re-

sulting in cirrhosis can produce cancers, not only primary liver cancers but cancers in general, particularly in the alimentary tract and in the lungs. All carcinomata, sarcomata, leukemias, Hodgkin's disease, and other malignancies are the result of liver damage caused by deficient food (malnutrition) or by chemicals added to the food (chemical compounds used for preservation of food, especially derivatives of tar), by dyes added to food, or by parasitic infestation, by alcoholism and drugs, by infections affecting the liver such as syphilis, by x-rays or radio-active substances."

The increase in cancer of the lung in recent years is explained in unusual fashion. Blond believes that smoking only causes a shifting to the lungs of the cancer caused by alimentary toxins, and that the mortality rate for all cancers in a certain population remains constant. Nicotine is not primarily a hepatopathogenic agent but it may have serious toxic effects on a previously damaged liver. If the liver is damaged and its detoxifying function is impaired, more alimentary toxins are carried to the hyperemic lung where they act as a local irritant, and thus shift the cancer to the lungs.

If these hypotheses should prove to be correct the prevention and even the cure of cancer should be relatively straightforward, even if not necessarily simple. One has merely to prevent liver damage to prevent the occurrence of cancer, and to treat the liver damage after surgical extirpation of the cancer. Blond explains that a patient may die six months after a radical operation on a relatively early cancer of the breast, because of relatively advanced failure of the liver. He states that the cure and the prevention of cancer will be possible only by the prevention of liver damage and the treatment of liver failure.

ADJUNCTIVE THERAPY OF CANCER BASED ON TREATMENT OF ASSOCIATED LIVER DYSFUNCTION

Blond (1) believes emphatically that patients who die with cancer of the breast do not die as a result of their cancers, but as a result of slowly increasing liver failure. On the other hand, regeneration as well as hyperplasia of a damaged liver is not impossible. If such regeneration occurs, a cancer may conceivably disintegrate without an operation and disappear. In this way, Blond explains the so-called spontaneous regression of cancer and the cures attained by quacks. He is of the opinion that the prognosis in the individual patient would be more reliable if liver function would be tested instead of distinguishing the different stages of the cancer.

Gerson (44, 45) pioneered in the dietary treatment of skin tuberculosis many years ago. The reports of improvement in seemingly hopeless cases of malignancy with the use of a modification of the diet seems hardly within the realm of possibility. Can all these cases be spontaneous regressions? If so, one physician has observed an unusually large number of these extremely rare cases. Perhaps Blond's explanation of the regeneration of a damaged liver is more tenable.

The diet used by Gerson was essentially, as follows:

1. Saltless (no salt, sodium bicarbonate, or other sodium-containing substances).

2. Fatless (no vegetables or foods containing fats, fatty acids or lecithin).

3. Poor in animal proteins (no protein for the first six weeks; then milk products in limited quantities).

4. Rich in minerals of the potassium group (selected fruits and vegetables rich in potassium).

5. Rich in carbohydrates from plants and fruits.

6. Abundance of fluids (vegetables, soup and various juices).

7. Rich in vitamins (Brewer's yeast, fresh fruit and vegetables as well as fruit juice and vegetable juices).

8. Rich in liver substances and enzymes (including defatted liver powder from young animals, 3–5 capsules a day, and injections of crude liver extract, 2 ml. daily at first then three times weekly and later twice weekly).

Thus the following substances are forbidden in this diet: salt, sodium bicarbonate and other sodium compounds, alcohol, coffee, tea, cocoa, chocolate, spices (with certain exceptions), pickles, smoked fish, sausages, all canned, preserved and bottled foods, white flour, refined sugar, candy, cake, ice cream, butter, all animal and vegetable fats, and nuts. Smoking is also forbidden. Meat, fish, eggs, milk, cheese and bread are temporarily forbidden.

At first glance this appears to be a starvation diet. Actually large amounts of raw and cooked fruit, fruit juices, vegetables, vegetable soup, and certain other foods are taken at frequent intervals during the day. The total daily caloric intake would easily reach 3000 calories. The menus cannot be listed here because of space limitations, but they are easily available in Gerson's published articles. I have no personal knowledge of any patients treated with the Gerson diet, but the claims merit consideration, with an open mind.

DISCUSSION

Alvarez (46) comments on the report of Nieburgs and his associates at the Cytology Conference held in Detroit. These investigators found widespread changes in the distant cells of patients who had a cancer somewhere in the body—suggesting that a person harboring a cancer may have a chemical circulating in the blood which can produce precancerous changes in distant cells. This phenomenon recalls to mind the "toxohormone" of Nakahara and Fukuoka (7–9).

Alvarez also mentions a microscopic section shown him by the great pathologist, H. E. Robertson. The patient had a carcinoma on the greater curvature of the stomach which had not spread either locally or distally, as far as could be determined histologically. Yet the cells of the colonic mucosa adjacent to the gastric area of involvement were markedly precancerous. Alvarez thought it was obvious that some chemical which was able to induce cancerous changes had diffused from the gastric cancer, through the apparently normal tissues, to produce a precancerous lesion in the colonic mucosa.

The "toxohormone" found in human tumors causes a marked reduction of liver catalase when injected intraperitoneally into mice. Circumstantial evidence of liver dysfunction is furnished by this observation and also by the finding of liver dysfunction in gastro-intestinal cancer (Pack and co-workers (35–38)) and the

results of tests by the present author and his colleagues (17, 42). These observations indicate that we should take into consideration the possibility of liver dysfunction in our plan of treatment for cancer patients.

Blond poses an even more intriguing concept—the possibility that liver damage is present before the development of the cancer, and that the cancer is able to develop because the damaged liver cannot detoxify the theoretical circulating toxins. These toxins may be exogenous or endogenous, and they themselves may cause the liver damage. Blond's theory is supported by the work of Orr on the production of liver tumors in rats by means of feeding butter yellow; degeneration of the liver cells, cirrhosis, and finally cancer of the liver results. The liver damage is present before the cancer develops. The work of Chan, McDonald and Cole (12) is also important in this regard. The clinical work of Trieger and his associates (40, 41) links the development of mouth and tongue cancer to the presence of liver damage.

We have almost reached the end-point in the development of surgery for the removal of cancers. Radiation dosage is becoming more and more powerful. In spite of these remarkable developments, the results leave much to be desired. We need to expend some of our energies on treating the host who bears the tumor.

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TOBACCO SMOKE AND THE ORAL MUCOSA.

A Pilot Survey of 279 Geriatric Patients

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Smoking as a carcinogenic factor is widely discussed in the scientific and popular literature. Certain investigators claim that smoking is an important causative agent in the development of cancer of the lung and cancer of the oral mucous membranes.

Several studies are in progress in an attempt to delineate the actual relationship between smoking and certain types of malignancy. The weight of the present evidence indicates that the relationship between smoking and lung cancer is causal and not merely a chance association.

Lewis (1) states that susceptible persons should not smoke excessively because of the danger of leukoplakia, and that leukoplakia may disappear after discontinuation of smoking.

Ryan *et al.* (2) came to the conclusion that further studies are necessary to prove whether irritants such as tobacco are causative factors in pathologic changes in the larynx.

Levin and co-workers (3) studied occupational factors together with smoking habits. According to these authors, certain occupations show a double incidence of lung cancer. Significant occupations in this respect are connected with metal construction work, free silica dust and excessive heat. Furthermore, the relative risk appears highest for heavy cigarette smokers. Other studies, however, also show a high incidence among pipe and cigar smokers.

Hazel *et al.* (4) reported on the deposition of different metals in the oral tissues from various types of dental fillings. Lain also (5) discussed lesions of the oral cavity caused by physical and physico-chemical factors.

However, the probability of cancer formation in different persons has not yet been established. In our group (6) we have noted that heavy smokers for fifty or more years may show no signs of malignancy, whereas other persons who have smoked only lightly for a few years may be stricken with cancer.

The role and the importance of additional contributory factors, such as physical, chemical and galvano-electrical actions, domestic and occupational exposure, inhalatory and other contact irritants (which by themselves also have cancerogenic or other irritative properties), have not been clarified. The role of inherited tendencies or individual weak points also requires elucidation. There is no satisfactory comparative study which indicates these interrelations in the over-all statistical, clinical and experimental picture (7, 8).

In the present study, the oral cavity of geriatric patients was selected as an area which would yield some significant data, because: 1) the oral cavity is

exposed to the highest concentration of smoke, fumes and other inhaled material; 2) it may or may not respond to such irritants with cancer or precancer formation; and 3) it is an easily available area for repetitive examination.

The purpose of the study was to attempt to answer some of the following primary questions:

1. Does smoking in itself produce cancerous changes of the oral cavity?
2. Does smoking predispose to cancer formation?
3. What is the incidence of identical pathologic changes in non-smokers?
4. What contributory factors may produce identical pathologic changes, alone or together with smoking (*e.g.*, carcinogenic fumes)?
5. What are the safety zones, if any, and the occupational hazards, with and without smoking?
6. What are the safety zones, if any, and the environmental non-occupational hazards, with and without smoking?

MATERIAL AND METHODS

The information for this investigation was gathered in the Skin Clinic of the Bird S. Coler Hospital and Home, which constitutes an ideal source of geriatric patients. Only a few private patients are included. Therefore the findings will, when our studies are completed, represent homogeneous material collected from laborers, skilled workers and lower-income white-collar employees who have lived in a large city or in the suburban areas for the greater part of their lives.

Of the 279 patients studied, 185 were smokers and 94 were non-smokers. The investigation was based on: a) interrelations between smoking and such factors as personal characteristics, mouth care, dental care, pathology and domestic and occupational environment, and b) the same factors in non-smoking patients.

RESULTS

A comparison of the smokers and non-smokers showed:

SMOKERS (185 SUBJECTS)		NON-SMOKERS (94 SUBJECTS)	
Sex		*Sex*	
Male	135	Male	35
Female	50	Female	59
Age groups		*Age groups*	
65–70 yrs.	36	65–70 yrs.	25
71–80 yrs.	87	71–80 yrs.	40
81–90 yrs.	51	81–90 yrs.	29
91– yrs.	11	91– yrs.	—
Smoking habits			
Cigarette			
heavy	67		
light	36		
Cigar			
heavy	9		
light	2		

SMOKERS (cont'd)	
Pipe	
heavy	29
light	3
Chewing	
heavy	—
light	3
Mixed	
heavy	28
light	8
Smoking history	
1–10 yrs.	6
10–20 yrs.	10
21–30 yrs.	21
31–40 yrs.	31
41–50 yrs.	38
Over 50 yrs.	79
Family history of cancer	12
History of syphilis	15
Coloring	
Blond (light skin)	102
Brunette (dark skin)	83
Occupation and dwelling	
City	
(indoor)	92
(outdoor)	41
Suburb	
(indoor)	28
(outdoor)	24
Tooth and mouth care	
Alveolar atrophy and pyorrhea	134
Different metal fillings	67
Bad dentures	34
No teeth	9
Cavities	117
Skin lesions	
Inflammatory	114
Precancerous	64
Cancer	18
ORAL MUCOSAL LESIONS	
Precancer of lip, tongue, bucca	24
Cancer of lip, tongue, larynx	3
Benign	6

NON-SMOKERS (cont'd)	
Family history of cancer	3
History of syphilis	4
Coloring	
Blond (light skin)	75
Brunette (dark skin)	19
Occupation and dwelling	
City	
(indoor)	60
(outdoor)	9
Suburb	
(indoor)	15
(outdoor)	10
Tooth and mouth care	
Alveolar atrophy and pyorrhea	51
Different metal fillings	20
Bad dentures	18
No teeth	5
Cavities	28
Skin lesions	
Inflammatory	65
Precancerous	2
Cancer	1 7 1
ORAL MUCOSAL LESIONS	
Precancer	14
Cancer	—
Benign	7

A comparison of the cases of precancer and cancer of the oral mucosa in the "smokers" group and the cases of precancer of the oral mucosa in the "non-smokers" group showed:

PRECANCER AND CANCER OF ORAL MUCOSA IN "SMOKERS" GROUP (27 CASES)	
Sex	
Male	23
Female	4

PRECANCER OF ORAL MUCOSA IN "NON-SMOKERS" GROUP (14 CASES)	
Sex	
Male	8
Female	6

Age group		*Age group*	
65–70 yrs.	4	65–70 yrs.	7
71–80 yrs.	14	71–80 yrs.	7
81–90 yrs.	6	81–90 yrs.	—
91– yrs.	3	91– yrs.	—
Smoking habits			
Cigarette			
heavy	10		
light	5		
Cigar			
heavy	2		
light	—		
Pipe			
heavy	5		
light	—		
Chewing			
heavy	—		
light	—		
Mixed			
heavy	4		
light	1		
Smoking history			
1–10 yrs.	2		
11-20 yrs.	5		
21–30 yrs.	10		
31–40 yrs.	9		
41–50 yrs.	—		
51– yrs.	1		
Family history of cancer	1	*Family history of cancer*	1
History of syphilis	4	*History of syphilis*	4
Coloring		*Coloring*	
Blond (light skin)	14	Blond (light skin)	9
Brunette (dark skin)	13	Brunette (dark skin)	5
Occupation and dwelling		*Occupation and dwelling*	
City		City	
(indoor)	10	(indoor)	6
(outdoor)	11	(outdoor)	3
Suburb		Suburb	
(indoor)	3	(indoor)	2
(outdoor)	3	(outdoor)	3
Tooth and mouth care		*Tooth and mouth care*	
Alveolar atrophy and pyorrhea	14	Alveolar atrophy and pyorrhea	9
Different metal fillings	10	Different metal fillings	3
Bad dentures	8	Bad dentures	5
No teeth	8	No teeth	—
Cavities	18	Cavities	10
Skin lesions		*Skin lesions*	
Associated with skin cancer and/or pre-cancer	12	Associated with skin cancer and/or pre-cancer	8

(Patients with more than one pathologic condition are listed in different categories.)

COMMENT

The results thus far indicate the following:

1. Leukoplakia of the oral mucosa developed in both smokers and non-smokers.

2. In the "smokers" group, a higher incidence of leukoplakia was noted for cigarette and pipe smokers.

3. The quantity of smoking was of greater importance than the duration of smoking.

4. The oral mucosa of the smokers in the oldest age group was not affected in most cases.

5. A familial history of cancer exerted no influence on leukoplakia formation.

6. Patients with a history of syphilis did not exhibit a higher incidence of leukoplakia.

7. Dental and oral hygiene was of great importance. Patients with bad dentures and different types of metal fillings showed a higher incidence of leukoplakia.

8. The incidence of leukoplakia was higher among men than among women.

9. Different degrees of pigmentation within the white race had no statistically significant influence on the development of leukoplakia.

10. Persons with outdoor occupations were more frequently affected than indoor workers.

11. a) In the "smokers" group, 3 malignant growths of the oral mucosa were found among 185 patients. b) In the "non-smokers" group of 94 patients there were no signs of malignant growths, but there were 14 cases of precancer.

This is merely a preliminary statistical study of a "captive" group from the Skin Clinic of one of New York City's institutions. Further studies of specific problems are in progress, as a much larger number of properly selected patients must be examined before conclusions can be drawn.

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THE COMPREHENSIVE DERMATOGERIATRIC INDEX: HEALTH QUESTIONNAIRE

(Preliminary Report)

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In this communication the Comprehensive Dermatogeriatric Index: Health Questionnaire (abbreviated C.D.I.) is described and the response to the questionnaire by a group of elderly patients, mostly women, is evaluated. The value of the C.D.I. and its further applications in the field of dermatogeriatrics is discussed.

Definition, purpose and description of the C.D.I.

The C.D.I. is an instrument similar to the Cornell Medical Index (1), but specialized in scope, which is designed to gather standardized information concerning skin disease in the older patient. It attempts to correlate the presenting dermatologic and medical history, patterns of living and environment, experience, family background and current physical economy. The questionnaire is constructed for easy review by the physician, and provides information about the total person.

The questionnaire is composed of 121 questions which the layman can easily understand and which may be translated into clinical terms. Emphasis is placed upon phrasing and the use of simple language. The questions are answered by circling the appropriate word (for example, Race: White, Negro, Oriental; Sex: Male, Female), or by indicating "Yes" or "No," or by filling in the required information (for example, What is your age——? Where were you born ————?). In addition, space is provided for the patient to describe in his own words his presenting dermatologic disorder or complaint.

The questionnaire is divided into 5 sections which are part of a complete dermatologic history. Seldom is it possible for an oral history to be as comprehensive. The number of questions in each section corresponds to the importance of the particular category. The following sections are included: 1) questions relating to general background or referring to the presence of a medical or skin disorder (for example, Do you have any kind of skin trouble now? . . . . Yes, No); 2) questions referring to the presenting skin disorder (for example, Do you have a growth on your skin? (wart, tumor, mole) . . . . Yes, No. Do you have a rash or other skin condition? (inflammation, infection, ulcer) . . . . Yes, No. Is there any itching or burning or smarting? . . . . Yes, No); 3) questions relating to the dermatologic history (for example, Have you ever been treated for your skin? . . . . Yes, No); 4) questions relating to the medical history (for example, Do you get pains in your legs after walking? . . . . Yes, No. Do you have frequent bowel movements? . . . Yes, No); and 5) questions relating to

functional or environmental disturbances (for example, Do people often annoy or irritate you? . . . . Yes, No). Questions are also arranged with regard to subject: the past dermatologic history, history of allergy, and food and drug histories appear consecutively. A list of the sections comprising the C.D.I. together with the number of questions in each group is shown in Table 1.

EXPERIENCE WITH THE C.D.I.

Administration

The C.D.I. was designed as a self-administered questionnaire. For testing purposes, 2 groups of patients were employed. Group I comprised 57 elderly men and women living in The Braker Memorial Home, which is under the medical supervision of St. Barnabas Hospital. They were allowed to complete the questionnaire by themselves with no preliminary explanation and no help. Group II comprised 47 elderly women residing in The House of the Holy Comforter. These patients were assisted in answering the questions by an aid who, although untrained in dermatology, was in daily contact with the patients as an occupational therapist. The time required for completing the C.D.I. varied; however, at least one hour was necessary, and sometimes more. The time required for taking the examination could not be determined in the self-administered group (Group I).

Response

The patients in both groups who were asked to complete the C.D.I. complied; a few hesitated but finally consented; some refused to take part. Reluctance in completing the form stemmed from various causes. Some patients were fearful that answering questions might in some way alter their status in the home, thinking that cause would be found to send them to the hospital for further investigation or examination, or financial resources might be questioned. Some were indignant at being disturbed and felt that they were being used in an experiment. Occasionally, specific questions were considered offensive. A few patients were annoyed by the length of the questionnaire and by having to answer questions which were restated for purposes of completion in different sections. In general, the questionnaire was accepted and taken in the spirit in which it was intended.

The responses to the questions which required an appropriate "Yes" or "No" (total 114) were tabulated on the basis of the type of answer: "Yes," "No," "Yes and No," no answer, and remark (when a write-in answer was substituted). Table 2 shows the raw scores obtained for both groups of patients. The response in each category of questions is indicated.

Productive replies were considered to be those which could be interpreted clinically or were historically significant. These answers clearly were "Yes," "No," or an affirmative or denying remark. Nonproductive replies were defined as lack of any answer to questions when a "Yes and No" was indicated, or an answer with a question mark or "I don't know." The percentages of productive and nonproductive replies for the entire series and the nonproductive responses for each section of the C.D.I. are shown in Table 2.

TABLE 1

Sections of the Comprehensive Dermatogeriatric Index

Section	Questions Referring to:	Questions	Number
A.	Vital statistics: age, marital status, etc	1 through 5a	6
	Background: present, past derm. and med. history	6 through 9	4
	Type of skin: dry, oily, pruritic	10 through 12	3
	Total		13
B.	Location and distribution	13 through 15	3
	Presenting condition: growth or dermatitis	16 and 17	2
	Onset	18 and 19	2
	Course of disease	20 through 29	10
	Clinical appearance	30 through 43	14
	Symptoms	44 through 50	7
	Total		38
C.	Dermatologic history:		
	Past history	51 through 55	5
	Physical reactivity	56 and 57	2
	Urticaria	58	1
	Family history	59 and 61	3
	Contact history	62 and 66	5
	Allergy	67	1
	Food	68 through 71	4
	Drug	72 through 76	5
	Total		26
D.	Medical history:		
	Eye, nose, throat	77 through 80	4
	Resp. system	81 through 84	4
	Cardiovascular	85 through 88 and 90, 91	4 2
	Cancer	89	1
	Gastro-intestinal	92 and 95	4
	Skeletal	96 and 97	2
	Endocrine	98 through 101	4
	Lues	102	1
	Total		26
E.	Functional and environmental	103 through 120	18
	Total		121

TABLE 2

Raw Scores for Patients of Groups I and II

Questions	Responses								
	Yes	No	No Answer	Remarks		Yes and No (Unprod.)	I Don't Know	Productive (%)	Nonproductive (%)
				Affirm.	Neg.				
Group I									
Section A (Nos. 6–12)	89	258	32	24	1	9			9.9
Section B (Nos. 14–50)	133	921	988	7			6		48.3
Section C (Nos. 51–76)	138	552	190	4		3	7		22.4
Section D (Nos. 77–102)	253	1095	89	6	3	1	4		6.5
Section E (Nos. 103–120)	254	591	109	25	19	13			61.7
Total (5,895)	879	3497	1408	45	23	26	17	75.4	24.6
Group II									
Section A (Nos. 6–12)	86	229	6	7	1				1.8
Section B (Nos. 14–50)	126	535	1049	6	2	20	1		61.4
Section C (Nos. 51–76)	246	752	204	14	1	5			17.1
Section D (Nos. 77–102)	250	891	49	30		1	1		4.0
Section E (Nos. 103–120)	263	528	33	16	5		1		3.9
Total (5,358)	971	2935	1341	73	9	26	3	74.4	25.6

Space was provided in the questionnaire for the patient to describe his presenting complaint. Twenty-six of the 57 patients in Group I, and 17 of the 47 patients in Group II contributed a self-appraisal. The following diagnoses or descriptions are examples of those which were offered: rash between folds of skin, psoriasis, no skin condition, warts on the neck, heat rash in summer, dandruff, herpes zoster, shingles, gold rash, iodine poisoning, quinine allergy, von Recklinghausen's disease, pimples on the face which come and go, wart at the edge of an eye, eczema probably due to nerves, winter itch, nodes on the ears, eruption similar to pimples, eczema since a teen-ager, itching between the fingers due to soap, and "the itch."

CLINICAL EVALUATION

Each questionnaire completed by the Group II patients was examined by a dermatologist and the information collected was translated into a clinical impression. Two or three minutes only were allotted for the interpretation of each form. The dermatologic diagnoses suggested in the questionnaire alone, and those arising over a 26-month period, were compared.

Forty-one of the 47 patients who completed the examination under supervision (Group II) gave a positive history which led to a dermatologic diagnosis. Of these, 23 indicated a disorder which had been previously diagnosed; 12 suggested

a skin disease which had been overlooked, and 6 focused attention upon a newly developed skin lesion. Six patients did not list a skin disease in the questionnaire; this coincided with negative findings in 5; only 1 who gave a negative history was observed to have a skin disorder.

Seventy-four diagnoses were suggested by the answers to the questionnaire; 34 of these were corroborated by the findings on dermatologic examination; 26 were not substantiated, and 14 occurred in patients who had not been examined during the previous twenty-six months or who had no dermatologic complaints.

Thirty-five patients indicated an underlying medical problem, current or past. These diagnoses (arthritis, diabetes, hypertension, sarcoma, cholelithiasis, renal disease and calculi) could be substantiated by the medical findings or the history.

A random dermatologic evaluation of the questionnaires completed by Group I patients compared favorably with the diagnosis based on the previous medical history and examination. Notations of skin disease were made by a resident in the department of internal medicine whose interest centered upon systemic disease rather than skin disorders. Many conditions were suggested by the questionnaire which had not been recorded; on the other hand, obvious skin disorders were found to be listed in both the questionnaire and the medical record.

COMMENT

The concept, organization and administration of the C.D.I. proved of value when measured against the response and information collected, although some changes in approach and presentation may be warranted.

Comparison of the productive responses elicited from Group I patients (self-administered test) and Group II patients (prompted) indicated that there was equal reliability. In Group II, 74.7 per cent of the responses could be used to formulate a clinical impression. In Group I (not coached) 75.3 per cent of the answers were useful. Although the value of the questionnaire as a self-administered instrument was in question at the outset, both means of administration seemed to provide an adequate response. The percentage of productive responses was similar in both groups. Group I patients, although elderly, had remained socially active and independent, whereas those in Group II were semi-invalids requiring institutional care. Both groups had a similar cultural background.

The questionnaire proved highly satisfactory, as shown in the responses by both groups of patients. The examination was particularly well received and the majority of answers were productive. The patients offered an illuminating evaluation of their particular dermatologic difficulties and supplemented this by a detailed, and in some cases exacting, description. Among the 17 Group II patients who presented no dermatologic complaint over a 26-month period of observation, the C.D.I. suggested further observations in 12 for fibroma, mole (seborrheic keratosis?), recurrent urticaria, food sensitivity, winter eczema, rosacea, wart (senile keratosis?), or contact dermatitis from wool; the absence of dermatologic disease was confirmed in the other 5. In only 1 patient did the questionnaire fail to reveal a previously diagnosed condition. Six patients among

TABLE 3

Cumulative "Yes" Answers

Number of "Yes" Responses	Group I, 57 Elderly Men and Women		Group II, 47 Elderly Women	
Below 10	18	32%	3	6.3%
10 or more	38	67.9%	44	93.4%
20 or more	17	30.3%	19	40.4%
30 or more	5	8.9%	8	17.0%
40 or more	3	5.3%	3	6.3%
50 or more	1	1.8%	2	4.2%
Inconclusive	1			

the 30 who had been under observation and had acquired a dermatitis, reported additional complaints in the questionnaire—senile xerosis, atopic history, food sensitivity, contact dermatitis, herpes zoster, eczema, seborrheic dermatitis, winter eczema or urticaria. There was a high rate of correlation between the impression gained from the questionnaire alone and the clinical findings. In 23 patients the proportion of answers to the C.D.I. questions referring to clinical features of the presenting condition and appraising subjective symptoms was somewhat lower than the average for the whole questionnaire. The highest proportion of nonproductive responses appeared in this area. Although a lay description of objective symptomatology is important in an oral medical history, probably questions in this category which cannot be modified or refined may appear ambiguous. Further evaluation of this phase of the C.D.I. in different age groups is necessary for clarification.

Although the number of patients who completed the C.D.I. test in both groups was too few for statistical consideration, cumulative "Yes" answers were calculated (Table 3). These values parallel those gathered from the Cornell Medical Index (1, 2). The significance of this finding should be elucidated by further testing in older and younger age groups.

SUMMARY AND PROVISIONAL CONCLUSIONS

This report describing the Comprehensive Dermatogeriatric (C.D.I.) Index and evaluating the response to the examination by a group of elderly people is preliminary. The results, however, are encouraging and suggest that such an instrument may prove of value in: 1) collecting standardized and comprehensive dermatologic and medical information in a group of elderly people, by means of a self-administered or coached questionnaire; 2) providing a source of information which can be easily and quickly reviewed by the physician; 3) detecting dermatologic disease with minimal effort and assistance; 4) enhancing dermatologic diagnosis by supplementing the history; 5) providing a research tool for the study of dermatogeriatrics; and 6) relating functional disease to cutaneous symptomatology in the elderly.

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FIVE-YEAR CONTROL OF AN "INOPERABLE" OBSTRUCTING CARCINOMA METASTATIC TO THE PORTA HEPATIS IN A 79-YEAR-OLD MALE

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The purpose of this presentation is to report an unusual instance of carcinoma of the inferior mandibular alveolus with metastases to lymph nodes in the region of the porta hepatis, which produced complete obstructive jaundice. The metastatic cancer was controlled for five years by combined palliative surgery and x-ray therapy. The patient eventually succumbed from an unsuspected new carcinoma of the sigmoid which produced metastases to the lungs. Despite extreme replacement of the lungs by cancer, there were no pulmonary symptoms until just before death.

CASE REPORT

H. W. P., a 79-year-old active chemical engineer, was seen in 1952 by a dentist who extracted a tooth from a necrotic area in the alveolus of the right mandible. A large fungating mass in the right bucco-alveolar gutter developed; this mass measured approximately 4 cm. x 3 cm. A biopsy on July 14, 1952, revealed a Grade II epidermoid carcinoma of the right mandible. A resection of the right mandible with dissection of the right neck was performed, and the patient made an uneventful postoperative recovery.

Six months later, marked jaundice developed. A history revealed intermittent bouts of clay-colored stools and abdominal pain associated with pain in the right shoulder. Jaundice had been noticed by the patient for two weeks. There was a weight loss of 15 pounds in one month, but no history of nausea or vomiting. For one week prior to becoming jaundiced, his urine had been dark and there had been one tarry stool. The findings on physical examination were essentially unremarkable except for a palpable, smooth, nontender liver extending 3 cm. below the right costal margin.

Laboratory studies on January 4, 1953 revealed a hemoglobin level of 14.5 Gm. per 100 ml., a white blood cell count of 10,500 per cu. mm. and a hematocrit of 48 per cent. The urine was dark with urobilinogen (present in 1:20 dilution) and also contained bilirubin. Occult blood was persistently present in the stools. The level of serum bilirubin was 30 mg. per 100 ml., and 80 per cent was direct-acting. Serum cephalin flocculation was 3-plus, and alkaline phosphatase activity was 2.9 Bodansky units. The concentration of serum urea nitrogen was 18.3 mg. per 100 ml., and total cholesterol 266.6 mg. per 100 ml., of which 50 per cent was esterified. The prothrombin time was 16 seconds. A liver biopsy, performed on January 6, revealed early portal cirrhosis with no evidence of infectious hepatitis or tumor.

On January 21, 1953, an exploratory laparotomy was performed, which revealed a huge mass involving the porta hepatis and compressing the bile duct. The mass could not be removed, so a modified Longmire-Sanford (1) short-circuiting operation was carried out; the jejunum was anastomosed to the free margin of the liver. The pathology report on the biopsy specimen from the mass in the porta hepatis was "undifferentiated carcinoma."

On January 30, 1953, a course of roentgen therapy was begun, and over a period of twenty-seven days the total air dose was 1600 r to an anterior and a posterior field through each port. The patient withstood the x-ray treatment well, and toward the completion of the course the jaundice had cleared, the stools were brown, and the patient was asymptomatic. He was seen in June 1953, at which time there had been a gain in weight of 15 pounds. His

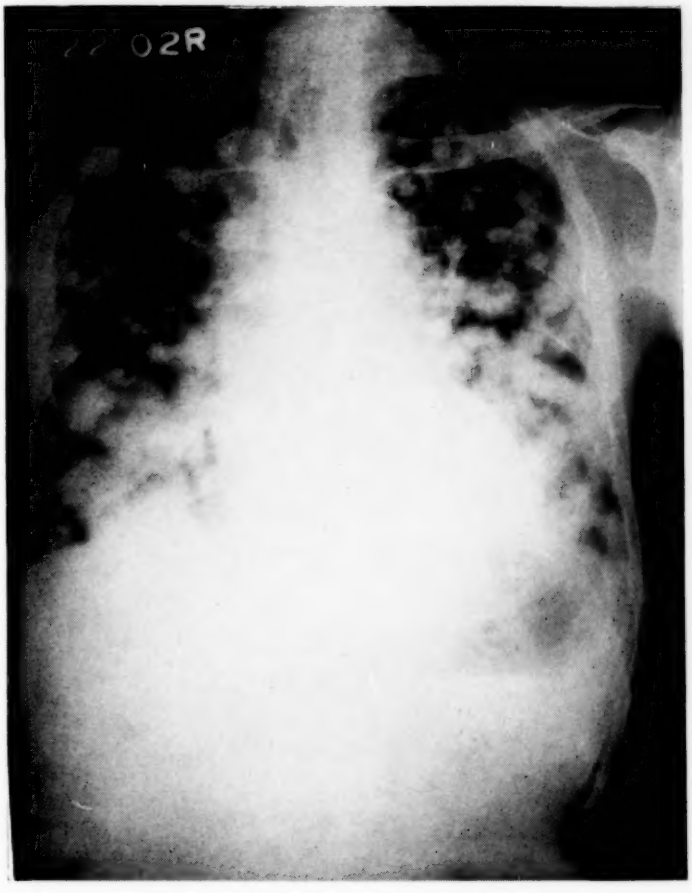

FIG. 1. Numerous metastases to the lungs from a primary carcinoma of the sigmoid. Note the extensive replacement of pulmonary tissue by the cancer.

appetite was good and a roentgenogram of his chest showed nothing abnormal. Physical examination did not show any evidence of residual or metastatic cancer. The patient was free of symptoms and "felt fine."

He remained well until October 26, 1958—five years and ten months after exploratory laparotomy and six years and three months after resection of the mandible. At this time he was 85 years old. He complained of generalized weakness, a 20-pound weight loss, abdominal distention, intermittent abdominal cramps and constipation of three months' duration, and dyspnea of two weeks' duration. He was admitted to the Hospital for Joint Diseases in marked respiratory distress. His blood pressure was 170/90 mm. Hg, temperature 98° F., respirations 46 per minute, and pulse 190 per minute. Physical examination revealed a chronically ill, cachectic man with diffuse, moist, crackling râles throughout both lung fields. The liver was 3 cm. below the costal margin and there was 2 plus pitting edema of both lower extremities. The patient was in a state of congestive heart failure, and he was treated accordingly. X-ray examination of the chest revealed massive metastases involving almost the whole lung (Fig. 1). Ten days after admission, a 5-millicurie dose of radioactive gold was injected intravenously. On the sixteenth day after admission the patient died. Autopsy revealed a primary adenocarcinoma of the cecum metastatic to the liver, lungs, spine and adrenal glands. (Figs. 2 and 3).

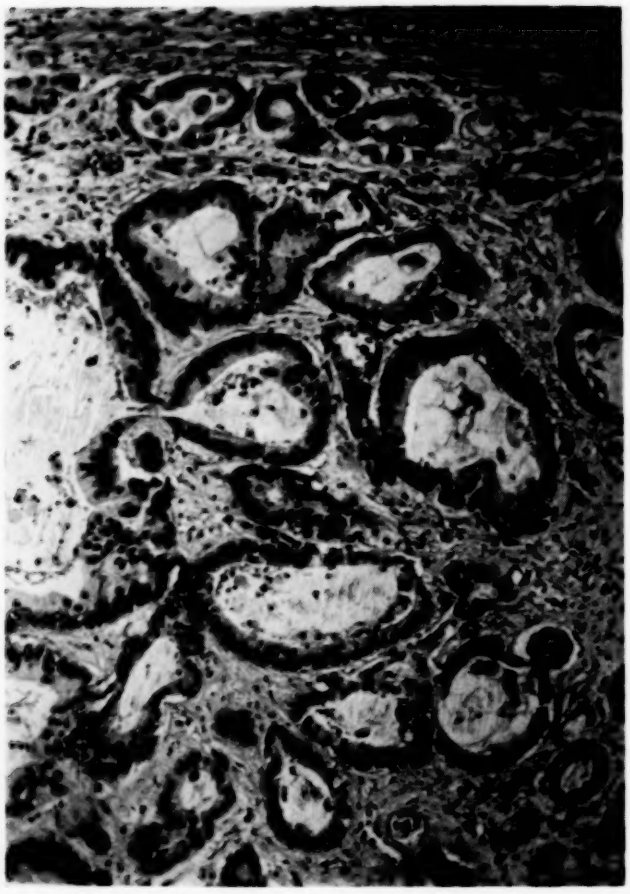

FIG. 2. Adenocarcinoma of the sigmoid, Grade II, which produced extensive metastases to the lungs.

DISCUSSION

Several features are demonstrated by this case:

1. Multiple carcinomas may occur in one patient.

2. Marked palliation often can be provided by orthodox procedures; thus old age should never be a deterrent to the treatment of cancer.

3. Lung tissue may be almost completely destroyed by cancer, without the production of respiratory symptoms.

This patient, at 79 years of age, underwent resection of the mandible and radical neck dissection for epidermoid carcinoma. The marked relief of symptoms afforded by this operation indicates that cancer therapy should not be denied any patient because of advanced age. Other than a mild cosmetic deformity on the right side of his face and neck, which the patient covered with a beard, he had no postoperative functional disability. At a later date metastases to lymph nodes developed in the region of the porta hepatis. This is an unusual phenomenon, as metastases from carcinoma of the mandibular alveolus to sites below the clavicle are rare. An exploratory laparotomy was performed despite

FIG. 3. Pulmonary metastasis from the primary adenocarcinoma in the sigmoid colon.

the severe state of jaundice and cachexia in an aged patient. He was treated vigorously. A by-pass procedure was carried out, whereby the jejunum was anastomosed to the liver for bile drainage; subsequently a course of orthovoltage x-ray therapy was given. Excellent palliation and complete control of the metastatic deposit was obtained for more than five years.

The patient refused to return for follow-up visits. Then at the age of 85, more than five years after the abdominal operation, he telephoned and simply stated that he felt "rotten."

On admission he was in a state of pronounced congestive heart failure. Roentgenograms revealed almost complete replacement of lung tissue by tumor. The respiratory difficulties dated back only three weeks, emphasizing the fact that marked involvement of the pulmonary tissue can occur with a paucity of symptoms. In this instance the symptoms did not develop as a result of the lung cancer, but rather as a secondary effect of the congestive heart failure.

An autopsy unexpectedly revealed a second primary carcinoma in the sigmoid colon, which was the source of the metastases to the lungs.

SUMMARY

A case report is presented of a 79-year-old man who was treated by orthodox measures (mandibulectomy and radical neck dissection in continuity) for extensive carcinoma of the mandible; this resulted in complete control of the local cancer. Metastasis to the porta hepatis six months later was aggressively treated by a short-circuiting surgical procedure plus x-ray therapy, following which there was complete symptomatic control for more than five years. Only then did the patient return because of symptoms due to a second primary cancer in the sigmoid with metastases to the lungs. The lungs had been almost completely replaced by cancerous tissue, yet respiratory symptoms had been present for only three weeks.

The good result from vigorous treatment of the mandibular carcinoma and its hepatic metastases emphasizes the fact that advanced age should never be a deterrent in determining therapeutic policy.

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RETIREMENT—GOOD OR BAD?

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"Ten dollars down, ten dollars a month—a nice easy way to buy a piece of land and retire—no rush, no schedules, no punch-clock, no bosses, just leisure time all day long to rest and fish and do nothing." What a life after the hustle and bustle of making a living! Now it's over and you can relax. What's over? The hustle and bustle, or your life? The general trend to retirement these days seems all wrong.

For the past few decades our national economy has been working overtime to retire both the working man and his boss, earlier and earlier in their lives. Corporation and business managements use early retirement plans more and more as an inducement to get and to keep good productive junior executives in their organizations. Unions are constantly striving for bigger and better pension plans and planned retirement communities. There is no argument whatsoever with provision being devised to guarantee financial security in old age. The bone I have to pick concerns more than a trend; it is the headlong, blind dash to earlier retirement from productive labor, for both the "pick and shovel" physical group and the "second vice president" mental group.

RETIREMENT

Effect on the individual

What is retirement? What does it mean to you? Most of the people I question stare at me blankly. Surely, I'm told, it's the time when one can sleep late, relax, and enjoy oneself with no more cares or responsibilities. But look about you at your retired friends or neighbors. There is the old man down the block puttering with his flowers for hours on end, whose meager conversation is so circumscribed as to be boring; the "retired" widow, whose main occupation (or rather preoccupation) in life apparently is to get the whole empty house cleaned at least once a day; the ex-machinist who spends morning and afternoon wandering the neighborhood, searching for another retired machinist to reminisce with; and the couple up the street who sit before the television set, one stupefied and the other hypnotized, while their muscles get cramped and their arteries get hard. What has happened to these people now that they are retired? They have ceased to live in a give-and-take world where they stimulate others and are stimulated in return. Their energies for living have run down like a clock someone forgot to wind, until one day it stops—and nobody cares.

Webster's Universal Unabridged Dictionary defines retirement literally as the act of being retired, *i.e.*, (*a*) withdrawn, secluded, (*b*) secret, private, (*c*) difficult to be seen, known, or discovered. It is almost an ideal description of the pitiful

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occupants of the "back wards" of our mental institutions where gracious custodial care is rendered to the numerous badly deteriorated schizophrenic and senile psychotic patients among our mentally ill population. This is not a coincidence. Retirement and mental illness in most cases belong in the same category, the former frequently being the precursor of the latter.

What are the effects of retirement? There are three main considerations. The most personal is the retiree's feeling of being "let out." Lately a good deal of literary and dramatic composition, based on psychologic and other analyses, has been offered to emphasize the importance of ego support in mental health. Ego support means prestige. It means compliments and respect. It means distinguishing one from the group for superior accomplishment in some respect. It is somehow associated with the joy of accomplishment, a sense of exhilaration; and most important and more basic, it means the reason for being alive, for being a human instead of a grain of sand or a gust of wind. A strong ego results in creativity and productivity, in law abidance and legality, in progress towards a better society. A weak ego results in a lackluster personality that invites denial and rejection by others, and insignificance—a bruise and an insult to one's being born. Lack of support to the ego produces neurotics, "beatniks" and malcontents.

Retirement means a loss of ego support. This results in depression and leads to withdrawal, which eventually becomes senility. How does this trail wind? It starts with a basic premise or proposition that the human psyche requires love and affection to develop and mature normally. It also requires love and affection, or a suitable substitute, throughout life, just as the physical body requires food and sustenance. The substitutes consist of such things as the daily accomplishment of working at a job and gaining recognition from superiors for good work, of winning awards or receiving raises in salary or position, and of being noted, with advancing years, as an authority, an expert or a highly skilled worker. Dr. Jack Weinberg, Clinical and Research Professor of Psychiatry at The Chicago Medical School, stated recently to the American Medical Association Planning Conference on Aging:

"The aging or the aged are people in a certain period of life and, as people, have the same qualities and needs that people at any life period have. They have the same needs as the child has, the young adolescent and adult—the basic needs of being wanted, of being loved, of being needed, of being productive, of being part and parcel of his environment, and belonging to a larger order of things."

Retirement, to the man who has spent most of his life climbing the stairs to "the top of the building," means that when he finally reaches his goal all he finds is an elevator waiting for a quick plunge to the street floor. Why is this? Again, Dr. Weinberg gives us the answer:

"There are certain American attitudes and values which can be called clearly American and it is those that operate against the needs of our aging population.

Now then, what are these value orientations that we have. There are basic things that people in every culture think about, certain values that they hold and what are they? They are answers to some specific questions that all human beings ask of themselves no matter

who they are—whether highly civilized or primitive. They ask such questions as, 'What is man's inherent nature—Is it good, bad, or is it both?' 'What is man's relationship to time—Does man value the past, does he value the present or does he value the future?'

Certainly each human being has a relationship to all three types of elements but the question is which of the dimensions is most valued.

The Mexicans, as an example, value the present. To them the present is very important. If you ask a Mexican to meet you at nine-thirty at a given place, then you, with your American watch to guide you, are going to be there at nine-thirty. However, he might be there at nine-thirty or even the next day at nine-thirty because in the meanwhile he may have found something which has caught his interest and, as a result, he will lose himself in it for the moment. Why should he give up that which interests him for some dubious appointment with you at nine-thirty in the morning?

In China the past is enormously important and so it is also in Britain and many other European countries.

However, what about our society? We are of course future-oriented. We know exactly what we are going to do, a week from now, a month from now, and even a year from now. We never get into anything unless we can ask the question and receive a positive response—'What is the future in it?' We are so busy planning for the future that when the future catches up with us and becomes the present we cannot enjoy it because we are again busy planning for you know what. We seldom find ourselves in a position of enjoying that which we do at the moment.

How then does this sort of attitude affect the aging organisms in our society? Obviously, they are a people without a future and, therefore, subversive to our culture. The doctors will state, 'How can you build a practice with old people—there is no future in it?' Therefore, we invest greatly in the young. Because of our future-mindedness we are a child-minded society and we will do anything for our future citizens."

What about those who can most afford to retire? They rarely do. Most physicians and lawyers and other professionals work until they die, although most could retire if they wanted to. Observe the Professor Emeritus who comes to the university office daily, though only for a half-day, and is still going strong at 90 years of age; or the President of the bank who just won't relinquish his grip, even though he needs a chauffeur to help him to his office, at 87 years of age. The list is interminable, and we all know such people. These folks are working because they want to and no one has forced them to retire. Yet, the most noteworthy thing is that *they still can work.*

Compare such a man to one retired by the rules of the company or by the expectations of his associates or clientele. Suddenly, overnight, he is shorn of all that is familiar, that is habit, and that is reason for being; lost in a desert dry of stimulation and excitement, devoid of challenge or demand, he becomes sullen, depressed, inactive, and then withdrawn. And *this* is the beginning of the end. Slowly (but sometimes, quickly), senile changes appear—the mild delusion, the short hallucination, the voice in the empty room, the momentary confusion, "What day is it?", "Why did I get dressed up?", "Everyone is against me." Personality changes occur first, then failures and accidents, and finally confinement in order to prevent injury to self or others. The Mental Health Societies of America have been one of the fastest growing types of health organization in the world during the past decade or so. And with good reason, when one considers the staggering amounts of the state and county budgets devoted to support of public hospitals for the care of the mentally ill. It is estimated that 70

to 80 per cent of all public hospital beds are occupied by the mentally ill, with a good proportion of them in the custodial group, meaning long-term care *and* expense. Senility shares this expense, for 1 out of every 3 people entering a mental hospital is over 60.

Effect on family and friends

The effect of retirement on the family and friends can be just as disturbing as on the retiree himself. It is commonly observed that many women cannot abide their husband's constant companionship; they become "nervous wrecks" (and vice versa, of course). The following letter was taken from "Column With a Heart" in the *Miami News*:

"Dear Eleanor Hart:

I am a confused wife who has a retired husband with nothing to do . . . no hobbies, no interest in anything but eat, sit, sleep and get up with gripes, aches and pains.

Our funds are small so we have to resort to TV for entertainment, but he goes to bed at 7:30 p.m., sleeps until 7 a.m. Everything bothers him. If I'm working, he can't wait until I leave, but looks for me at mealtime.

If he hears people talking or children playing outside, he gripes. If I watch TV after he has gone to bed, he doesn't want singing or musical shows turned on.

Please tell me what is wrong with a person like that? There is a 15-year difference in our ages, and he has been retired two years.

Ask him to find something to do around the house, and he says he is retired, only lying around and waiting to die."

It is unneccessary to belabor the point that while the one who is unable to fill the void left by retirement struggles to maintain his ego support, his family and friends share the burden along with him. Living in the past, he becomes a bore, with his repetitious stories of bygone days. Gone is the patience to be with children, and so he becomes misunderstood and rejected by them. The rapidly increasing older population (most of whom are not gainfully employed) creates a bigger and bigger strain on the financial reserves of the working family members. This, in turn, leads us to the third major effect of present-day retirement, namely, the effect on the national economy.

Effect on the national economy

Over and over one reads of absenteeism in industry and the effect on national income of the loss of man-hours of production, due to this or that disease, or to labor strikes. But what about the lost labors of our retired population, most of whom are physically able to continue working at retirement time? Here is a vast source of skilled and experienced and reliable energy being allowed to seep out of our manpower pool. Men who supervise goodwill industries and sheltered workshops for the elderly, retired or handicapped, repeatedly stress the desirability of hiring such persons. Take the case of Paul Klein, whose story was printed in *Modern Maturity*, January 1, 1960:

"'There is the problem of the small business to which proper executive direction means success or failure, and there is the tragedy of the man over 60 who is forced into retirement simply because of his age.'

The 45-year-old manufacturer says he owes the success of his two firms, Forty-Two Products and Executive Toiletries, makers of hair dressing, shampoos and lotions, to his practice of hiring executives after some other company has retired them.

Klein has been trying to get other industries to adopt his idea.

'The biggest crime in business today is automatic retirement age. These men then are left just to waste their lives away when they really want to work.

'I started my business after years with another firm,' he said. 'After getting all the details wrapped up and the papers signed, I thought I was in business.

'But suddenly I had a horrible thought, I realized that all my experience was mainly that of salesman. I had no conception of how to put together the materials for my products.'

Klein said he figured that somewhere there must be a retired executive or two who would help him get his new business started. He hired Chris Nelson, 61-year-old chemist, and Kirkley Sinclair, 71-year-old comptroller. Both had been with top national firms.

'The older, retired man isn't afraid to give his knowledge away,' Sinclair said. 'The young man is still trying to reach the top, is very reluctant to pass on to anyone all of the tricks of the trade he has managed to learn. You can't blame him. It's just self-preservation.

'But the old guy has already been there. He's not trying to go any place. So he finds that the one way to perpetuate himself is to teach young men what he has learned. It gives a life purpose and it actually prolongs the lives of our older citizens.'"

Older people who are working do two things: they increase income and they decrease taxes.

COMMENT

Chronologic age is no indication for retirement. Who would deny the contributions of older people to our society? We do not "retire" our great men at 65 years of age—or at any other age. Eddie Cantor, now 64, recently wrote:

"Retire at 65? Who? Why? Supposing Winston Churchill had retired at 65, and what about the new Germany under Adenauer at 83, and the present savior of France, DeGaulle, 68? What wouldn't any important corporation in America give for the service of one Bernard Baruch?

"Maurice Chevalier at 71 is a bigger hit than he's ever been. Ed Wynn started a bright new career at 70, turning from one of the great comedians of show business to a fine sensitive, dramatic actor."

Branch Rickey, at 77, was named president of the Continental Baseball League. The man who broke organized baseball's color line by signing Jackie Robinson thirteen years ago, had to be convinced that he was the only man for the job because the league required a man of his great dignity, integrity, respect, proven talent, progressive ideas and pioneer background.

Herbert Hoover, at 85, has one word for the secret of longevity and health: *work*. He says, "Those who retire without some occupation spend most of their time talking about their ills and pills."

These names have been well known to us for a long time, but consider the meteoric rise of "Grandma" Moses, who at 99 has already produced over 1,000 paintings worth from $1,000 to $4,000 each; she only started to paint at age 78. Suppose, like most other folks, she did *not* have this talent—what would have happened to her? In her own words, as reported by Robert Peterson in *Modern Maturity*, "I'd have raised chickens or I'd sell pancakes."

Everywhere in nature, things exist according to the universal law that for every action there is a reaction. When the stimulus does not occur, there is no response. The human mind must, like all other living things, be continuously stimulated; otherwise it will atrophy and die. Unless there has been a start early in life to cultivate retirement activities that will provide adequate strength and stimulation, one will become, as Webster puts it, "withdrawn, secluded, difficult to be seen, known or discovered."

PSYCHOLOGIC PROBLEMS OF GERIATRIC PATIENTS

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Rare is the human who is adequately prepared to meet the emotional problems associated with age, illness, enforced idleness, and approaching death. As Tolstoy, with great insight, observed in *War and Peace* (1): "At the approach of danger there are always two voices that speak with equal force in the heart of man: one very reasonably tells man to consider the nature of the danger and the means of avoiding it; the other even more reasonably says it is too painful and harassing to think of the danger, since it is not in man's power to provide for everything and escape from the general march of events; and it is therefore better to turn aside from the painful subject till it has come, and to think of what is pleasant. In solitude a man generally yields to the first voice; in society to the second."

In our American society, which has been described by Slavson (2) as a "free group culture," it is probable that the majority of members have, indeed, turned away from the painful subject of old age and illness, with the exception that some have attempted to provide for their material welfare. Few have paved the way for maximal satisfaction of the basic emotional needs under the vastly changed circumstances. In loneliness, idleness and solitude, many of the disabled aged who still possess their intellectual facilities relatively intact, ponder with discomfort the emptiness and barrenness of their present lives.

PSYCHOLOGIC PROBLEMS

At least partial satisfaction of some of the patient's individual emotional needs some of the time is of paramount importance if the goals set by any member of a rehabilitation team are to be achieved. An unhappy, disillusioned, apathetic, poorly motivated patient resigned to his present fate because he perceives neither reason for, nor hope of improving, manages to negate the best rehabilitative efforts of the staff.

Physical versus emotional needs

Hospitals designed primarily for physical care, tend by their very nature to treat patients on a biologic basis and to center the patients' activities around bodily functioning. Though the members of the staff do much more than provide services and therapy designed to preserve or improve physical function, most of them are necessarily so busy performing their traditional duties of diagnosing, treating, bandaging, feeding and exercising, that they may regard the patient as an ulcerated stomach, a paralyzed left arm, a set of untrained bowels, or a case of hemiplegia. With the pressure of duties, it is easy to forget that these disorders affect various aspects of a whole person who has all the emotional needs common to humanity, but with few facilities for gratifying these needs.

This biologic segmental orientation makes it much more difficult to reach the patient as a living, thinking human being, and naturally impedes utilization of unique opportunities to help him gratify his emotional needs. Moreover, since a patient's perception of himself is affected significantly by his perception of the reactions of others toward him, he tends to regard himself as merely a body with aches, pains and infirmities rather than a being with personal goals and motives. Because his activities are centered around the gratification of bodily needs and the minimizing of pain, the more uniquely human activities such as warm personal relations, creativity, and independent thought, are increasingly relegated to subsidiary positions. Thus, one of the major sources of fuel for rehabilitation—the patient's own aspirations—becomes less available. The patient himself concentrates primarily on bodily self-preservation, a goal which in all likelihood could be achieved with greater probability and less effort if the patient were to concentrate also on meaningful personal goals.

Achievement

Almost all of the disabled and hospitalized aged are confronted with new barriers in their attempts to satisfy their emotional needs, though the type of barrier and its rigidity vary from patient to patient. Since many geriatric patients have outlived, or worse still have been rejected by, friends and relatives, some of them may not have one person who loves them or who will accept their affection. They may lack a feeling of belonging and of being a wanted member of any group. Families are often outspokenly unwilling to take them back into their homes, the work world does not need them, and they have no social life apart from the hospital. Even in the hospital, where they may have a feeling of continuity if not of being personally wanted, they may be transferred from ward to ward, or confronted with the prospect of discharge to a nursing home, to another institution or to a rejecting family. Objectively, the accomplishments of such aged patients are extremely limited, because of physical or intellectual disabilities, and just as frequently because of lack of motivation. Why should they strive to produce when no one cares? Moreover, what they do achieve, whether it be in terms of M.A.T.[1] projects, or being able to walk a little farther, is likely to be judged by them in terms of "what used to be." Hence what is a real achievement in terms of present limitations, may be perceived by the patient as being less good than it ought to be. With limited accomplishments, the feeling of achievement and the recognition and praise from others are not forthcoming, so other needs are unsatisfied. We, who are not old, disabled and hospitalized tend to perceive the patient from the pinnacle of our own power and often miss opportunities to praise him for his efforts, endurance, fortitude, cheerfulness, persistence in spite of overwhelming obstacles, his smile in spite of pain, and the many other praiseworthy characteristics which pass unnoticed. It is much easier to notice and comment on the negative features which interfere with our efforts to propel the patient toward our designated goal for him,

[1] Manual arts therapy.

than to notice and praise the commendable assets which the patient, perhaps with no small effort on his part, contributes.

Hope

Human beings have a marvelous capacity for enduring devastating hardships in the present, if they can hope for improvement in the future. The present life of the majority of the disabled aged is besought with hardships, some of which we cannot even realize, because we are not likewise old, disabled, unwanted and helpless. For many of them the hope for better things to come is not available as an alleviator of the grimness and bleakness of the present. Some, fortunately, have a firmly founded religious conviction that in a life hereafter there will be eternal happiness. For a greater number, it would seem (although this has not been fully investigated), such hopes are vague or nonexistent. What realistic hopes have they for the immediate future? Increased physical well being? Productivity on a job? Warm personal relations? Increased independence? Compliments? Visits from loved ones? The sober truth is that many of our disabled aged, when they are wakened in the morning, realize that today they have nothing to look forward to—that today can be expected to be as bleak, painful, long and lonesome as yesterday and the day before and tomorrow and all the tomorrows, and may bring, instead of relief and improvement, progressive impairment.

Independence

Every human being has a need for a certain amount of independence. Although medical institutions are designed in part to enable the patient to increase his independence by improving his bodily functioning, the necessary rules and regulations stringently limit such independent action. There are schedules for appointments, meals, baths, and sometimes even toileting. Formerly independent persons, because of their physical disabilities, may be as dependent as tiny children for the satisfaction of their basic physical needs—a predicament which from their point of view is not analogous with that of infancy, because of their former independence. With ingenuity, opportunities can be found to enable the patient to exercise some independence—or barring that, to let him think so. A patient who is given an opportunity to make decisions when it seems important to him, is more apt to demonstrate some of the necessary initiative in striving for his own rehabilitation.

Self-esteem

Perhaps the major psychologic need of all humans is for self-esteem. The man who cannot like himself or respect himself will almost certainly be forced to resort to drastic measures, often socially nonacceptable or self-defeating, to bolster his own self-concept. The chief ingredients of self-esteem are satisfaction of psychologic needs such as affection, belonging, achievement, a feeling of usefulness, recognition, hope and independence. Many geriatric patients are weak, dependent, rejected and useless, so they are sadly lacking in self-esteem. The

reactions to this lack are varied and only too familiar: unreasonable demands, temper tantrums, unnecessary dependence, suspiciousness, bragging, self-pity, weeping, obstreperous behavior, and frequently excessive apathy. The picture is, however, unnecessarily bleak. A patient's self-esteem can be bolstered by the staff with much less effort than that required to cope with the undesirable behavior that is an expression of a damaged ego. Such minor devices as praising a patient's fortitude in pain, accepting the fact that life is indeed rough for him at present, noticing his consideration of another patient, recognizing that he was once a competent engineer or salesman, or commenting on his good grooming, can add appreciably to the patient's concept of himself as a unique individual worthy of the respect of others and hence of his own respect.

Individual differences

In the management of the disabled aged, the extreme variability in personality, past background and intellectual attributes of patients should be considered. Scientists have concluded that the range of individual differences in psychologic characteristics within age groups increases with age. Thus, it is impossible to describe a patient's connative or cognative status as a function of his age. Geriatric patients in a hospital represent a dependence-independence continuum that is not only physical but also emotional and intellectual, involving such factors as memory, emotional lability, self-control, hostility, aggressiveness, self-pity, determination and rigidity. Moreover, the elderly disabled include a wide variety of patients such as former highly successful business or professional men; day-laborers; drunkards; ne'er-do-wells; the happily or unhappily married, as well as spinsters and bachelors; those who are either loved by, out-lived by, or totally rejected by their families; those who are highly motivated to retain their personal identity; and those who are almost completely resigned to leading a vegetative type of existence. The quality of intellectual functioning of patients housed in a single geriatric ward has been known to range from a level lower than that of an average 4-year-old child to a level equal to or superior to that of the average doctoral candidate. Obviously it is not reasonable to apply only one set of rules for motivating or managing the rehabilitation of patients who demonstrate such important individual differences.

There is still another area in which individual differences should be considered. For example, when a patient has to undergo total laryngectomy, the nurses are advised, both before and after operation, to be cheerful and optimistic about the patient's ability to learn esophageal speech. This advice is not tempered by considerations such as Levin's (3) declaration that the successful learning of esophageal speech depends upon intelligence and the will to learn, nor the fact that most of the patients who undergo total laryngectomy are elderly and thus age and/or organic brain damage may have impaired learning ability and intellectual functioning. Some patients have a low intellectual endowment initially, many have never consistently applied themselves to any difficult learning task, and others, because of their current life situation are not highly motivated to learn. Such factors should be taken into consideration prior to informing a pa-

tient cheerfully that he will be able to speak again. Individual differences in other personal attributes are equally significant in planning for the patient's rehabilitation and in motivating him to participate actively in his own maximum recovery.

REHABILITATION

What can be done to help the elderly disabled to meet some of their psychologic needs? Actually much is being done by most members of most rehabilitation teams and much more can be accomplished. A technique used on one geriatric service might be of interest.

Geriatric Council

Several months ago, in this VA hospital, 9 patients selected jointly by the psychologist, social worker, physician and head nurse were invited to join a "Geriatric Council" which meets for one hour twice a week. New members are admitted at times when discharges, deaths or transfers from the ward have occurred. During the meetings, the patients are free to discuss any topic of interest to them. These topics have included complaints about hospital procedures and particularly about nursing assistants; reactions to hospitalization; old age; sickness and death; hopes for improvement and discharge; politics; why people drink, steal, make unreasonable demands and disturb others; the good and bad marriages of the participants; recitals about children, previous careers and childhood reminiscences; and pride in M.A.T. projects.

Since the initiation of the Geriatric Council, several changes have been noted. At first the patients had to be coaxed to come, and during the meeting, they addressed most of their comments to the leader. Now, they come very willingly, and those who can walk often wheel those who need assistance. Conversation between patients has increased appreciably. The initial sessions were full of complaints about the hospital in general, and particularly about the attendants. Currently, complaints are rare and, when made, indicate increased understanding and tolerance, *e.g.*, the attendant obviously could not gratify a particular demand instantaneously because he was otherwise engaged in something of greater importance. The participants are recognizing the difficulties and handicaps of others. Realistic encouragement is not uncommon, nor acceptance of the fact that the life of another is rough. Not only has the interaction of the participants increased on the ward, but there has been increased interaction with nonparticipants. The participants, on occasion, have suggested ways in which they might make life more pleasant for persons with disabilities different from their own.

Book Club

More recently, another group called the "Book Club" was initiated to bring together very intelligent patients, some of whom tended to isolate themselves on the ward which they had perceived as populated with uneducated, unintelligent or degenerated patients. In this group, the discussions (which usually start

with a book such as Gibbon's *Decline and Fall of the Roman Empire*, Sandburg's *Abraham Lincoln* or Freud's *Dream Analysis*) have ranged through ancient history, the American political situation from the Boston tea-party to the current election, the Cuba and Congo situations, psychoanalysis and neurotic illness, and comedians and stage plays of the 1920's. Discussions are continued on an individual basis between meetings, and recently each member asked for permission to invite a guest member to the group.

Effect of group sessions

Group sessions help to gratify the psychologic needs of the patients in several ways. Each patient is treated as if he were a unique individual worthy of respect. His comments and opinions are listened to. He belongs; he is welcomed when he arrives and is told that he is missed if he doesn't come. He is given recognition and praise; his M.A.T. projects and the pictures of his grandchildren are admired. Each one recognizes that the other is putting up a good fight in spite of difficulties. Small improvements are commented on by both leader and members. A wise statement, a good suggestion, or a witty remark are treated with full appreciation. The patient is given the opportunity to complain, and his right to do so is recognized. Tension is discharged in a protected atmosphere. His need for independence is in a small measure gratified by permitting him to attend or not attend sessions as he sees fit, and by a rule that no guest or new member will be admitted without the consent of all other members. His horizons are broadened in human contacts, realization of the sufferings of others, and opportunities for self-expression. His self-esteem is enhanced by being treated as a person with a past, present and future who belongs to the group, who has admirable qualities, and who has some rights for self-guidance and expression. The group sessions, though not designed to effect a basic change in personality structure, do enable one staff member working simultaneously with many patients to help them to satisfy some of their emotional needs.

Psychologic as well as physical aspects

In the over-all management program for the elderly disabled, the patient must be considered as a total functioning unit, with psychologic as well as physical needs. Our elderly disabled are neither minds nor bodies, but minds *and* bodies. Persons suffering from excruciating pain may be concerned with little other than the need to allay the pain. Likewise, persons suffering from terrible emotional wounds may not be good candidates for purely physical rehabilitation.

SUMMARY

Geriatric patients have the basic emotional needs common to all human beings, and in addition may be confronted with new barriers to the satisfaction of these needs, and new problems associated with physical decline, approaching death, family rejection and feelings of uselessness.

Each chronically ill, elderly patient has to deal with emotional or psychologic problems of tremendous personal significance, which affect the outcome of all

rehabilitation efforts. Emotional needs or drives do not disappear with age, physical weakness or living in an institution. Elderly patients have, like all other people, the need or desire for affection, belonging, hope, achievement, recognition, independence, variety, and particularly for self-esteem; however, in old age the opportunities for satisfying these needs decrease, and, with deprivation or lack of satisfaction, the perceived need may be intensified.

Some techniques which may be used by members of rehabilitation teams to help the elderly disabled are suggested. Special attention is given to group activities.

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ALLERGIC REACTIONS INVOLVING THE CARDIOVASCULAR SYSTEM AS THE TARGET AREA

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Physicians who treat or who are in contact with a large number of geriatric and other patients are aware of the increasing number of adverse reactions to the various types of medicines. Since allergy is such a common condition and because sensitivity may affect any organ of the body, it is important for physicians to be constantly aware of the possible harmful effects of the medications which they are prescribing. This danger is highlighted when one considers the almost unlimited number now in existence plus the influx of some 400 new and reformulated drugs, pharmaceutical specialties and biologicals which are constantly being poured into the market each year. There is reason to believe that the trend will increase in future years unless some solution is found to this complex problem. That this trend may be reversed is suggested by the tightening of the Food and Drug regulations and demands for more explicit field work. Nevertheless, there should be further study in order to determine which of these drugs and how many of them are causing cardiovascular allergy.

It is now generally believed that sensitivity may affect any organ in the body. This study, however, will focus attention on the cardiovascular system as the so-called shock organ. When the target area is the heart and blood vessels, the reaction can be violent and dangerous. Allergens may disrupt the functions of the heart and slow down the flow of blood through the arteries and veins. Many observers have already published a large mass of clinical evidence describing allergy of the vascular system. In addition, unpublished observations by many clinicians leave no doubt that a number of cardiovascular deaths may be attributed directly to the action of various allergens. Until recently, many of these fatalities have gone unsuspected and were thought to be due to independent pathologic entities. It is, therefore, of considerable clinical importance to recognize these conditions early, so that proper management may either avert or modify many cardiovascular complications.

Allergy includes all types of hypersensitivity. It may exist in the host as a result of heredity, or it may be specific in response to hypersensitivity to various bacterial and fungal agents. Other forms frequently encountered in clinical practice are those caused by sensitivity to various drugs and serums. Innumerable reports may be found in the literature. The offending antigen may be introduced into the body by direct contact, ingestion, inhalation, or even by various types of injections. Finally, allergy may be due to a variety of physical agents such as heat and cold.

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Hypersensitivity causes the release of histamine by the tissues of the body. The resulting allergenic reaction may be immediate, as in anaphylactic shock, or it may be delayed for hours or even days. The sensitivity reaction often varies with the species of animals. For example, in the guinea pig, death is produced by bronchial spasm; in the rabbit, arteriolar spasm results in acute cor pulmonale causing death by heart failure; in the dog, death results from a tremendous venous engorgement caused by the muscular contraction of the hepatic vein; and, in man, the mechanism may be similar to that in the guinea pig or dog (1).

Bernreiter (2) reports the case history of 74-year-old man who was given 600,000 units of penicillin prior to a cataract operation. Within a few minutes he went into a state of anaphylactic shock with typical respiratory distress and collapse. The electrocardiogram taken within fifteen minutes showed involvement of the myocardium and the coronary circulation with typical auricular fibrillation, multifocal ectopic beats, intraventricular conduction disturbance, severe coronary insufficiency and injury to the posterior wall of the left ventricle. The patient recovered, and his electrocardiogram returned practically to normal. This mechanism may explain sudden death due to anaphylactic shock involving the cardiovascular system. Foster and Layman (3) report a case in which electrocardiographic changes, simulating those of myocardial infarction, occurred during the course of an urticarial reaction to drugs. The electrocardiogram showed complete auriculo-ventricular dissociation with an auricular rate of 94 and a ventricular rate of 50. In addition, the tracing showed typical signs of posterior myocardial infarction. The case was tentatively diagnosed as painless coronary occlusion. When the electrocardiographic tracing returned to normal twelve days later, it was decided that the changes were due to an allergic reaction involving the cardiovascular system, and not to myocardial infarction.

There has been a tremendous advance in our knowledge of the allergic mechanism during the past few decades. Recently, it has been found that the incidence of such reactions is about twice the usual estimate and that it affects about one-third of all children up to the age of 14 years. No general statistics have been compiled regarding the incidence of cardiovascular allergy in the general population.

IDIOPATHIC MYOCARDITIS

There is a certain group of diseases of the myocardium in which the cause is unknown; they have therefore been classified under the heading of "idiopathic myocarditis." This waste basket includes the following types: Fiedler's, isolated, interstitial, acute or subacute productive, fibrous, circumscribed, diffuse, pernicious, granulomatous, and possibly others. This large group represents cardiopathies of not just one, but of various unknown etiologies. Every attempt should be made by more careful clinical, laboratory and histologic studies to remove as many as possible of these from the list of the unknown.

There is no doubt that in at least some of these cases, allergy plays either a primary or a dominant etiologic role, and they should be classified as allergic

myocarditis. Gore and Saphir (4) classified 1,402 autopsy cases from the Army Institute of Pathology during the recent war and found 105 cases of myocarditis due to sulfonamide hypersensitivity. Saphir (5), in 1941, reported 240 cases of myocarditis in a series of 5,626 consecutive autopsies; 15 were cases of Fiedler's myocarditis. Scarpelli *et al.* (6) described a case of nonspecific isolated myocarditis in which the inflammatory reaction was confined solely to the myocardium. There were no demonstrable pathologic changes throughout the rest of the body. He stated that although the cause was unknown, he had reason to believe that hypersensitivity, either to drugs or chemicals, played a role. Wells and Sax (7) and French (8) reported cases of diffuse isolated myocarditis resulting from allergy to sulfonamide chemotherapy. Waugh (9) described a case of sudden death in a patient with interstitial myocarditis following hypersensitivity to penicillin. Franz (10) observed myocardial lesions which he believed were due to hypersensitivity to epinephrine. Sikl (11) reported 2 cases of myocarditis following treatment with neoarsphenamine, which were probably due to allergy.

Fiedler's myocarditis

Lieberman (12) cited 2 cases of Fiedler's myocarditis due to an allergic condition following a viral infection of the upper respiratory tract. Jaffe (13) stated that Fiedler's myocarditis is very common in Venezuela, and that the myocardial lesions are due to an allergic reaction to the necrotic myocardial tissue resulting from pre-existing infections such as syphilis, bilharziasis, necatoriasis, or Chagas' trypanosomiasis, or from beri beri; all these types were morphologically identical. Along these same lines Dressler (14) described a myocardial infarction syndrome that occurs in 3 per cent of patients following an acute myocardial infarction. He asserted that the symptoms might be due to sensitization by the necrotic myocardial tissue. Cortiocosteroids afford dramatic relief in these cases, but anticoagulant therapy may cause fatal cardiac tamponade.

The collagen diseases

The collagen diseases comprise another group in which the etiology is obscure, but in which allergy may play an important part. This group is so classified because the diseases mainly attack the mesodermic tissues, which include those of the cardiovascular system. Among these disorders are rheumatic fever, rheumatoid arthritis, polyarteritis nodosa, lupus erythematosis disseminatus and diffuse scleroderma. Others possibly are serum sickness, dermatomyositis and thrombo-angiitis obliterans. Here again various etiologic agents may be involved in the damage to the cardiovascular tissues.

There is good evidence that, in some of these conditions, the damage is caused either directly or indirectly by the action of various allergens which invade the body. A close study of these various unknown collagen disease entities is very important. The clinical practitioner who is in a position to observe the entire cycle has a better vantage point than the hospital clinician or consultant from which to correlate the biologic changes that take place as the disease progresses. The usual procedure, at this time, is to rely upon the experience and knowledge

of the internist. However, should the data for differential diagnosis include the observations of the patient by his practitioner, supplemented by the experiences of the allergist, many of these conditions could be more properly correlated and classified.

BODY TISSUES

It has been postulated by Criep (15) that blood itself may act as a shock organ. This is a new concept and immediately suggests the possability that allergy plays an important role in the production of various blood dyscrasias. Criep's work and theories open up a vast new field in the concept of allergy. He believes that every tissue of the body under certain suitable circumstances may become involved in the reaction of hypersensitivity. He especially mentions allergy that involves connective tissue, blood cells, platelets, and thyroid tissue. It may even involve the testes, uvea, lens and the central nervous system.

TOXINS VERSUS ALLERGENS

Whether a reaction is toxic or allergic in nature may be very difficult to decide. It is important to distinguish the allergic reactions from those due to protoplasmic poisons such as emetine which, as Panting (16) has pointed out, may produce myocarditis.

Toxins, whether microbic, vegetable or animal in origin, may be antigenic and elaborate specific antitoxins. Since protoplasmic poisons of various types produce tissue death, the resulting necrotic tissue may in turn cause various toxin-antitoxin reactions in the host.

It is common practice to consider reactions to digitalis preparations as toxic in nature. The question of digitalis allergy has never been clarified. Many prominent cardiologists have never had occasion to record instances of allergy due to digitalis preparations. Nevertheless, there is no reason why this condition should not occur. This problem will be discussed in a future study.

PULMONIC HEART DISEASES

The heart and the blood vessels may be affected indirectly by the allergic state. Patients with chronic allergic bronchial asthma, may experience the gradual development of permanent and irreparable damage to the respiratory system with the narrowing of the arteriolar bed. Chronic cor pulmonale results from reduction in vital capacity and the development of pulmonary hypertension. Acute cor pulmonale occurs when there is a sudden narrowing of the arteriolar bed, such as may happen during anaphylactic shock.

CARDIAC IRREGULARITIES DUE TO FOOD ALLERGY

It is well known that extra systoles and other cardiac arrythmias may follow the ingestion of allergenic foods. As a rule, allergy may develop through frequent and prolonged contact with eggs, milk and wheat. However, any food may cause a violent allergic reaction. During the acute attack, the eosinophils may increase in number. For example, Richardson (17) reported 3 cases of rapid heart rate

due to milk allergy. He also described a case of tachycardia due to cigarette smoking in a 35-year-old unmarried woman, and another of tachycardia with premature contractions in a 53-year-old married woman. In the latter case the offending allergen was unknown but the attacks were controlled with chlorpheniramine maleate (Chlor-trimeton) in a dosage of 4 mg. three times a day.

August and Zohman (18) reported the case of a 15-year old-boy with paroxysmal nodal tachycardia followed by inversion of the T waves. He died suddenly on the second day of hospitalization. At necropsy, myocarditis of unknown origin was found. One week prior to his entry into the hospital, he had eaten 25 to 40 bananas. Two days later he had become sick and had vomited three or four times. Several hours later, while asleep, he had awakened suddenly and noted a rapid heart beat which had persisted until he was admitted to the hospital. Bananas have been known to cause many allergic reactions, and no tissue is exempt. In many patients, attacks of tachycardia and other arrhythmias due to ingestion of allergenic foods can be prevented by elimination diets.

ALLERGIC ARTERITIS

Allergic reactions in the blood vessels beyond the heart occur more frequently than is realized. For example, the use of tobacco may induce anginal pain by causing vascular spasm or thrombosis in badly sclerosed arteries. This has been demonstrated in many patients who manifest a positive reaction to the skin test for tobacco; in some, antibodies have been demonstrated by passive transfer; in others (sensitized persons), tobacco smoke has caused cardiac disturbances.

Many of the arrhythmias have been associated with some sort of sensitization, and erythema nodosum and erythema multiforme are known to occur in association with the allergic state.

ALLERGENIC CAPILLARY PURPURA

Between 1949 and 1958, the hospital records of Yale Medical Center included those for 43 cases of capillary purpura due to allergy or drug reaction. The following are 4 typical case histories:

Case 1

A 2½-year-old white girl was admitted to the hospital on August 29, 1958. The chief complaint was a rash of twenty-four hours' duration. On the day before admission, she had a sore throat and fever, ate poorly and was fretful. On the night before admission she was seen by a private doctor, at which time the findings were suggestive of streptococcal meningitis. An early rash was noted on the lower extremities and also some insect bites. She was treated with 80 mg. of penicillin every four hours. The parents did not clearly recall whether she was given aspirin. Following this, she appeared relatively afebrile and in good spirits but her rash was pruritic and she scratched it. The rash began to spread and, on the advice of the physician, she was admitted to the hospital.

At the time of admission, she presented as a well developed, well nourished, unhappy white girl who had a slight cough and a rash but did not appear ill. Her temperature was 37.8° C., and her pulse was 110. Positive physical findings were limited to the skin and to the throat. The skin showed several varieties of rash over the lower extremities, where they were grouped mainly about the ankle and the dorsum of the foot. The areas between

the toes and around the ankles were red, and there was no blanching on pressure. This rash was papular; the papules were relatively flat and ranged in size from 3 x 3 mm. to 1 x 2 cm. Other rashes were maculopapular, with lesions measuring 0.5 x 0.5 cm.; some were larger, with a central papular elevation. These appeared in places to be vesicular, and elsewhere crusted; they blanched slightly, but not completely with pressure. Elsewhere, the rash had been scratched and was ulcerated. The soles of the feet had a blotched, macular, purpuric appearance. The purpuric macular and maculopapular areas which had been scratched were on the buttocks and the lower abdomen. Maculopapular erythematous nonblanching and blanching lesions measuring 2 x 2 cm. were present on the wrists and upper back. There was a 5 x 5 mm. area of impetigo low on the back of the neck. The palms, face, neck, chest and arms were clear. The feet and ankles were swollen and somewhat tender, but there was no pitting edema. A strawberry birthmark (4 x 10 cm.) was present over the sacral region. The tonsils were enlarged and cryptic, with scattered gray-white exudates over the crypts. There were no other abnormal physical findings.

A smear of the petechial contents revealed lymphocytes in excess of polymorphonuclear leukocytes, and occasional eosinophils. No bacterial organisms were seen. A peripheral blood smear revealed abundant platelets. The impression on admission was: allergic purpuric rash.

The admission laboratory examination showed a hemoglobin level of 12.2 Gm. per 100 ml., hematocrit 36 per cent, white blood cell count 10,800 per cu. mm. with 41 per cent polymorphonuclear leukocytes, 50 per cent lymphocytes, 3 per cent monocytes, 2 per cent young lymphocytes and 3 per cent atypical lymphocytes. There was a fully adequate number of platelets (smear). The urine was normal. A nose and throat culture showed Hemophilus influenzae; a blood culture showed no growth. The Rumpel-Leede phenomenon was not present. Clotting was normal. Streptococcal studies were initiated, and at the time of discharge C reactive protein was reported as 3 plus. Repeated counts showed leukocytes, 15,500 per cu. mm. with polymorphonuclear predominance (65 per cent), and an adequate number of platelets in the smear. Repeated urine cultures showed no growth.

On the day following admission, the rash darkened and no new lesions appeared. Chloramphenicol (Chloromycetin) was started because of the findings in the nose and throat culture. Four days after admission, the rash began to spread and involved both ears, the face, conjunctiva and palate. The patient appeared well, however. A platelet count on the day of discharge was 490,000 per cu. mm., and an adequate number of platelets was seen in the blood smear. The discharge diagnosis was allergic purpura.

Case 2

This 5-year-old boy was admitted March 7, 1956, with a chief complaint of red spots over the face. Headache, cough, and slight malaise had been present for one day prior to admission. On the afternoon of the day of admission, the first episode of vomiting had occurred, in association with some bleeding from the nose. With the third episode of vomiting, a red rash developed over the eyelids and cheeks, and was described by the patient's physician as petechiae. The patient had been quite well prior to this illness.

The past and family histories were noncontributory.

On physical examination the pulse was 110, respirations 28, temperature 38.6° C., and blood pressure 106/70 mm. Hg. The child appeared to be in no acute distress. Many small petechiae were noted over the face, especially over the upper eyelids and the cheeks; some were also noted in the axillary area. There was evidence of epistaxis in the left nostril. The pharynx was moderately injected. The neck was supple. Many small cervical nodes were palpable. Examination of the heart revealed a grade II blowing systolic murmur, audible along the left sternal border. There was no enlargement of the liver or spleen. Neurologic examination revealed nothing abnormal.

Laboratory data: At the time of admission the hemoglobin level was 13 Gm. per 100 ml., and the white blood cell count 8,000 per cu. mm. with 63 per cent leukocytes and 33 per cent

lymphocytes; the number of platelets in the smear was normal. Rumpel-Leede's phenomenon was marked on admission. The clotting time was six minutes. Urinalysis on three different occasions yielded negative results. Two days after admission, the platelet count was 224,000 per cu. mm. The Rumpel-Leede sign had disappeared. Clotting time was seven minutes, and clot retraction was normal.

Treatment was started with 600,000 units of procaine penicillin intramuscularly twice a day. The patient was afebrile on the second day. No further petechiae were noted, and there was some clearing of the petechiae over the face. A nose and throat culture showed no growth. The patient was discharged, improved, on March 10, 1956. The discharge diagnosis was anaphylactoid purpura.

Case 3

A white male child aged 2 years and 3 months was admitted on June 15, 1958, with a rash on both legs, which were also swollen. He had been well until three weeks prior to admission when he had been brought to the Emergency Room with a swollen knee. The knee was examined by x-ray, and an Ace bandage was applied. Two days later, the dorsum of the left hand was noted to be swollen, tender, and painful on movement. X-ray examination revealed soft-tissue swelling. At the Pediatric Clinic the following day, examination of the blood and nose and throat cultures showed nothing abnormal. The child was treated with adrenocortical steroids. On the day prior to admission, an electrocardiogram was normal. A diagnosis was made of either Henoch-Schoenlein purpura or rheumatic fever. Four days prior to admission, the rash on the legs started (according to the mother) as a pimple, and developed into a large red blotch. From its initial site on the back of the right leg, it spread to the left leg and then to the soles and sides of both feet. These red areas were itching and tender. The right hand was painful for four or five days prior to admission. However, on the day of admission, the swelling disappeared. There was no history of rash on the stomach or face, no abdominal pain, no fever, and no nodules under the arms. The mother had noted one episode of slight swelling at the sterno-manubrial joint which lasted for one hour and then disappeared. The child was reported to be slightly sensitive to sunlight. There was no history of butterfly rash. In the previous month he had eaten strawberries for the first time, and also canned Franco-American spaghetti. These were thought to be involved in the allergic reaction.

The family history was pertinent, in that there was a history of hay fever in one aunt.

The physical examination findings upon admission were essentially negative except for enlarged cryptic tonsils which, however, were not injected. In the neck there was anterior cervical adenopathy and one small, right posterior cervical node. Over the heart, a grade I systolic murmur could be heard over the precordium with maximal intensity between the third and fourth intercostal spaces. The pulmonic second sound was greater than the aortic second sound. The heart was not enlarged. The important physical finding upon admission was the fading ecchymosis over the posterior region of both legs and calves and over the right thigh. The joints did not appear to be swollen, although the right knee was slightly tender. The impression upon admission was allergic purpura probably of the Henoch-Schoenlein type.

Laboratory data: The hemoglobin level was 9.4 Gm. per 100 ml., hematocrit 34 per cent, erythrocyte sedimentation rate 10 mm. per hour and white blood cell count 12,900 per cu. mm. with 65 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes, 3 per cent monocytes, and no eosinophils; the platelet count was 472,000 per cu. mm. Urinalysis on June 23, 1958 revealed 2 to 3 red cells and 1 to 3 white cells per high-power field, but on June 27, 1958 the findings were negative. Rumpel-Leede's sign was not present. Blood cultures showed no growth. Tests for enteric agglutinins yielded negative results, as did streptococcus studies. Bleeding time and clotting time were within normal limits. The level of serum nonprotein nitrogen was 27 mg. per 100 ml. A growth of beta hemolytic streptococci was found in a throat culture.

The boy was given 400,000 units of penicillin twice a day for ten days.

Case 4

A 10-year-old boy was referred to the Grace-New Haven Community Hospital for admission on May 8, 1958, because of urticarial purpura and edema of four days' duration. He had been well up to three days before admission, when giant urticaria had developed. The following day, the urticarial areas had become purpuric and there was edema of the face, hands and feet accompanied by slight fever. There was no vomiting or diarrhea, and no complaints of pain. On the day before admission, the patient's edema and urticaria began to recede and the purpuric spots became localized to the buttocks and legs. On the day of admission, the edema and urticaria had disappeared but the purpura was still visible on the posterior aspect of the thighs, on the buttocks and on the abdomen.

Both the patient and the family had a past history of allergy.

On admission the blood pressure was 100/68 mm. Hg. The pulse, respirations and temperature were normal. The patient was active, alert and responsive. The positive physical findings were limited to slightly enlarged posterior cervical nodes, which were shotty and discrete, and purpuric spots on the thighs, knees, ankles, abdomen and buttocks. There was no gross edema. The spleen was firm and could be palpated one and a half fingerbreadths below the left costal margin. No other abnormalities were found on physical examination.

Laboratory data: A complete blood count, platelet count, bleeding time, clotting time, and clot retraction time were all normal. The Rumpel-Leede phenomenon was not present. Nose, throat and blood cultures showed no bacterial growths. Results of tuberculin tests were negative.

The diagnosis was anaphylactoid purpura.

ALLERGIC DEGENERATIVE ARTERITIS

Arteritis, both acute and chronic, probably has multiple etiologic factors. The condition is usually secondary to a heterogeneous group of diseases, but it may be primary, as in the case of thromboangiitis obliterans, periarteritis nodosa or cranial arteritis. Present opinion is that allergy plays an important part in the production of certain vascular degenerative inflammatory conditions, and that the allergy is associated with a wide range of substances. The evidence indicates that the allergic necrotizing vasculitides may be caused by such substances as sulfonamides and antibiotics, administered for the treatment of some less formidable disease. These allergic conditions include hypersensitivity angiitis, temporal angiitis, allergic granulomatous angiitis, periarteritis nodosa and perhaps rheumatic angiitis. Miale *et al.* (19) reported 2 cases of acute panarteritis in patients with allergy; in the patient with allergic dermatitis, the diagnosis was made early, the medication was stopped, and the patient recovered quickly. It would appear that a variety of antigens may react to cause severe vascular damage in patients who are in a hypersensitive state for one reason or another.

Cury *et al.* (20) described a case of allergic granulomatous angiitis in a patient who had a history of chronic uveoscleritis and papilledema, which progressed to atrophy of the globe. Pathologic examination disclosed a necrotizing type of angiitis permeated by eosinophils. Another case of hypersensitivity angiitis was reported by Edge *et al.* (21). In this patient, the condition developed as a result of a sensitization to penicillin and streptomycin. The patient died suddenly during treatment with cortisone. Another case of periarteritis nodosa in infancy was reported by Adelson (22). He pointed out the relationship of the destructive arteritis to penicillin allergy.

ALLERGY INVOLVING THE VEINS AND LYMPHATIC VESSELS

Very little is known concerning the action of allergens on the veins and lymphatic vessels. However, there is no reason why such allergy should not exist. The veins, like the arteries, have a muscular layer; the only difference is that the veins have thinner walls due to the smaller amounts of muscle and elastic tissue. It must be kept in mind that the veins have three coats, and that they are capable of responding to chemical stimuli, as pointed by Franklin (23) in 1937. Since then very little attention has been given to this phenomenon, and there is no doubt that many reactions occur and go unrecognized. In some cases the spasm could be produced by hypersensitivity.

Allergy of the lymphatic vessels likewise has received little attention. These vessels are also capable of allergenic spasm, since they are developmentally an offshoot of the venous system and structurally have a middle coat composed of very fine elastic fibers and smooth muscle. Both the endocardium and epicardium have elaborate networks of lymphatic vessels which eventually join and empty into the mediastinal system.

Phlebitis has received little systematic attention because the surgeons, physicians and various specialists have been interested only in specific aspects of this subject. There are two types of phlebitis, infective and the noninfective, and each may or may not be associated with thrombosis. Phlebitis may exist as a separate entity, as in trauma, thrombophlebitis, idiopathic recurrent thrombophlebitis and phlebitis migrans, or it may follow as a complication of various diseases such as typhoid fever, influenza, gout, icterus neonatorum or splenic anemia. The role of allergy, if any, is not known but there is no reason to suppose that the necrosis of the venous muscular layers found in phlebitis may not be due to the action of allergens, as in arteritis.

SUMMARY

In approaching the problem of cardiovascular allergy from the diagnostic viewpoint, the most important factor is an awareness on the part of the physician that allergy may be involved wherever trouble exists in the body. Many diseases affecting the cardiovascular system may be explained on an allergic basis. Familiarity with the biology of the disease and its clinical manifestations, together with a careful history, physical examination, skin tests and laboratory determinations should help in making a diagnosis. If a patient with cardiovascular disease has a personal and family history of allergy and if his symptoms are in conformity with its nature, then allergy should be considered in the differential diagnosis.

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Abstracts of Current Literature

THERAPEUTIC TRIAL OF A NEW ORAL DIURETIC.

Beanlands, D. S., and Shane, S. J. *Canad. M. A. J.* **84:** 91 (Jan. 14) 1961.

Five patients with refractory edema were treated with Hygroton. Two had atherosclerotic heart disease with congestive heart failure, 1 constrictive pericarditis, 1 chronic rheumatic heart disease with mitral insufficiency and congestive heart failure, and 1 congestive heart failure of undetermined origin. The dosage varied from 100 to 800 mg. per day. Hygroton produced a marked diuresis in 2 patients and a moderate diuresis in 3 patients who previously had not responded to chlorothiazide, hydrochlorothiazide, flumethiazide, and mercurials. The weight loss was no less than 12 pounds in each patient. Hygroton had a selective effect on sodium and chloride excretion; it caused as much as 400 mEq. of sodium to be excreted in twenty-four hours. Potassium excretion diminished in 2 patients in comparison with that resulting from other diuretics previously, remained unchanged in 1 patient, and increased slightly in 2 patients. The peak diuretic effect occurred forty-eight to seventy-two hours after administration. One patient had nausea and vomiting that could be controlled with chlorpromazine. There were no other side-effects and no evidence of bone marrow depression. It is concluded that Hygroton is a potent diuretic.

GASTROINTESTINAL HEMORRHAGE AFTER ABDOMINAL AORTIC OPERATIONS.

Cordell, A. R.; Wright, R. H., and Johnston, F. R. *Surgery* **48:** 997 (Dec.) 1960.

Fistulization between the intestinal tract and the abdominal aortic prosthesis is a common cause of late graft failure and usually occurs at suture lines which are contiguous with bowel loops. Fistulization can occur with any type of prosthesis and even after endarterectomy. Any massive gastro-intestinal hemorrhage after an abdominal aortic operation should be considered of aortic origin until proved otherwise. Prompt suspicion of diagnosis and early surgical intervention are required if patients with such fistulas are to be saved. Possible means of preventing the fistulas include selection of manufactured prostheses rather than homografts, meticulous suture technique, peritonealization of suture lines and prosthesis if possible, interposition of living tissue between bowel loops and grafts, and keeping size discrepancy of host to graft at a minimum. (From authors' summary.)

STUDY OF BACTERIAL ENDOCARDITIS. COMPARISONS IN NINETY-FIVE CASES.

Friedberg, C. K.; Goldman, H. M., and Field, L. E. *A.M.A. Arch. Int. Med.* **107:** 6 (Jan.) 1961.

The recovery rate in 95 cases of bacterial endocarditis was 83 per cent compared with 66 per cent in an earlier series. Rheumatic heart disease was definitely or probably present in 79 cases. Five cases were classified as acute. There was little difference in the recovery rates among patients with positive and negative blood cultures. There was a higher incidence of congestive heart failure and cerebral embolism with hemiplegia in patients with negative blood cultures—50 compared with 19 per cent. The incidence increased as the delay in diagnosis and treatment exceeded two weeks. The peak incidence of bacterial endocarditis was in the sixth decade. There was a greater incidence of mortality in patients past age 50 years. Seven of the 10 deaths occurred in patients who had had symptoms longer than four months prior to therapy. This report and others indicate that the incidence

of recovery is far below what can be accomplished with antibiotics. Improvement in the rate can be effected and serious complications reduced by early diagnosis (preferably within two weeks of onset) and treatment. Accurate diagnosis, made early enough to permit taking blood cultures and to initiate treatment within a few days, is possible on the basis of minimal criteria—the presence of unexplained fever for longer than a week (preferably ten days) in a patient with an organic cardiac murmur. When the blood culture is positive, therapy is based on the nature of the offending organism and its sensitivity to antibiotics. Treatment can be started while awaiting the result of blood culture studies and sensitivity tests. Approximately 80 per cent of the causative organisms are sensitive nonhemolytic streptococci or moderately resistant nonhemolytic streptococci or enterococci. As trial therapy before the organism has been identified, treatment may be started with 10 million units of penicillin and 2 Gm. of streptomycin per day in order to control nonhemolytic streptococci and many staphylococci. If a satisfactory clinical response does not take place in two or three days, the penicillin should be increased to 50 million units, which should be effective against nonhemolytic streptococci and enterococci not sensitive to the small dosage; streptomycin is continued. Should this regimen fail after two days, then 3 Gm. of vancomycin per day should be administered intravenously in divided doses to combat a possible resistant staphylococcus. If these regimens fail and blood cultures remain negative, then the organism probably is resistant to generally employed therapeutic regimens, or the diagnosis is in error. A decision must then be made whether to use empiric therapy while trying to prove a diagnosis of bacterial endocarditis or to find some other cause for the symptoms.

THE EARLY DIAGNOSIS OF PROSTATIC MALIGNANCY BY THE USE OF P^{32}.

Haskin, M. E.; Wagner, M. L.; Ivker, M., and Widmann, B. P. *Am. J. Roentgenol.* **85:** 99 (Jan.) 1961.

A screening test was devised for measuring the differential absorption of radioactive phosphorus by benign and malignant prostatic tissue. The differences were measured by a Geiger-Müller probe inserted into the rectum over the area of the prostate. Count rates above 50 per cent of those for supposedly normal tissue were taken to indicate malignancy. In the examination of 29 patients, microscopic examination confirmed the screening interpretation in each case. An analysis of variance showed the intrinsic variability of the malignant group to be six times that of the benign group so that the difference between them could not be due to chance. The test is valid only when normal tissue is present. Nodules are ideal for evaluation by this method. The time at which the procedure was performed after injection was not critical. The highest readings were obtained in ten to twenty minutes. The most reliable and reproducible results were obtained after twenty-four to forty-eight hours. The count rates also could be duplicated with greater accuracy during this period. Limiting factors consist of the following: the range of the P^{32} beta rays in tissue, and the fact that the lesion must be within 5 to 6 mm. of the examining finger in order to be detected by the probe. Some improvements are needed in the probe used, in order to guard against erroneously high or low readings and changes in the counting area. A properly designed probe would have a pancake-type tip, sensitive in only one plane and having a high sensitivity in the beta range of P^{32}. A flexible stem would be desirable. The test described is potentially accurate, simple, and should prove a reliable diagnostic aid in detecting early prostatic malignancy.

GROWING DOWN. A NEGLECTED ASPECT OF AGEING.

Hughes, T. *Practitioner* **186:** 241 (Feb.) 1961.

It is estimated that the average man loses ½ inch in height every twenty years after he has attained maximum height. The shortening is caused by wear and tear, and for the most part by the absorption of cartilage (especially of the vertebral column but also of joints of

the lower limbs), exaggeration of slight deformities (*e.g.*, kyphosis, lordosis and scoliosis), and habitual faulty posture. The structure of the vertebral bodies makes them more likely to collapse than other bones since there is no layer of compact bone to enclose them and separate them from their cartilages. The aging process in the vertebral bodies may be painful. Displaced intervertebral disc has most often been thought to be responsible but it probably occurs with less frequency than has been thought. Another likely cause of pain is narrowing of the vertebral foramina due to shortening of the vertebral column. Inflammation of the nerve roots between the intervertebral foramina and the cord has been postulated as the cause of sciatica with the sequel of radicular adhesion formation. Another painful disability in the elderly caused by shortening of the vertebral column is overriding of the lower ribs on the iliac crest causing pinching of the intercostal nerves or sometimes disarticulation of the eleventh rib. Prophylaxis should begin in youth and include stretching exercises and a correct sleeping posture. Treatment of low backache with sciatica consists of saline injection into the epidural space using 200 ml. or more and injecting via the sacral hiatus by means of a lumbar-puncture needle and syringe. Suggested treatment of overriding of the twelfth rib on the iliac crest is subperiosteal filleting of the rib or a portion of it.

PROGESTATIONAL AGENTS IN THE TREATMENT OF CARCINOMA OF THE ENDOMETRIUM.

Kelley, R. M., and Baker, W. H. *New England J. Med.* **264:** 216 (Feb. 2) 1961.

Twenty-one patients with a pathologic diagnosis of adenocarcinoma of the endometrium, previously treated by hysterectomy or local radiotherapy or both, were treated with progestational agents. These were: aqueous suspension of progesterone, progesterone in oil, and 17-alpha-hydroxyprogesterone caproate in dosages of 150 to 1,000 mg. per week. Treatment periods varied from one month to four and a half years. Many patients experienced a sense of well-being, increased appetite, and increased vigor during treatment. Minor fluid retention and a sterile abscess at the site of injection in some instances were the only complications. An objective response occurred in 6 patients, accompanied by symptomatic relief. This response lasted for nine months to four and a half years. Five of the patients had regression of pulmonary metastases, and 1 of them regression of local disease in addition. The sixth patient had only a local recurrence. Three of these 6 patients now have died, 1 had a second remission, 1 is in a state of remission during continuous therapy, and 1 has progressive disease. Of the 15 patients who failed to respond, all except 1 died of progressive disease, although a few had showed subjective improvement. The mechanism of action of progesterone in carcinoma is not known. There was no evidence of its conversion to other types of hormone. The major effect was thought to be a direct local one similar to changes in normal or hyperplastic endometrium in response to progesterone. Luteinizing hormone was not measured but it possibly may be involved through changes in its level. This work appears to have demonstrated another example of a target-organ lesion that temporarily retains its hormonal identity and responsiveness despite neoplastic transformation.

THE USE OF THIORIDAZINE (MELLARIL) IN AGED PEOPLE.

Kral, V. A. *Canad. M. A. J.* **84:** 152 (Jan. 21) 1961.

Thioridazine was given in an average daily dosage of 70 mg. to 12 elderly patients with senile psychoses, 14 with cerebral arteriosclerosis with psychotic manifestations, and 11 with functional psychoses (depression, 7; manic phase of manic depressive illness, 2; and late paraphrenia, 2). These patients (mean age, 80.8 years) were residents of a home for the aged and the severity of the psychotic conditions was less than that usually seen in mental hospitals. The individual dosages varied from 20 to 200 mg. daily. The total dosage averaged 13.6 Gm. and the duration of treatment 217 days. Adjunctive therapy was given as needed but no other tranquilizing agents were used. The 7 patients with agitated depression re-

ceived imipramine to combat agitation. Eighteen patients had a good result, and 11 benefited moderately, whereas 8 showed no improvement. The result was considered good when a restless and agitated patient grew quiet and able to participate in activities of the home. It was considered moderate when the patient became manageable and cooperative although he did not participate in group activities. A good effect was noted in 7 of 12 patients with senile psychosis, in 7 of 11 functional psychoses, and in 4 of 14 psychoses with cerebral arteriosclerosis. The degree of improvement appeared to depend upon the severity of the clinical condition. The tranquilizing effect of thioridazine usually was apparent within twenty-four hours. Patients lost their restlessness and agitation. The drug did not interfere with thought processes. In patients with confusion of thought before treatment, the condition was not aggravated, but improved because of decreased restlessness and agitation. Thioridazine caused no improvement in depressive mood in patients with a depressive condition. With the dosages used there were no changes in neurologic status except for an increase in neurologic signs in 2 patients with arteriosclerotic parkinsonism. Some patients who received 25 mg. three to four times daily occasionally fell, although they did not experience dizziness. Their blood pressure on these occasions had decreased by 20 to 30 mm. Hg. Both this complication and occasional drowsiness ceased when the dosage was reduced. Thioridazine is well suited to the treatment of mental disorders of the older age group in moderate dosage and with proper precautions.

EVALUATION OF ANTIDEPRESSANT-TRANQUILIZER COMBINATION IN OFFICE PRACTICE.

Lentz, R. E. *Clin. Med.* **8:** 75 (Jan.) 1961.

Parstelin tablets containing 1 mg. of trifluoperazine and 10 mg. of tranylcypromine were evaluated in 45 women and 10 men (average age, 47 years) with mixed depression and anxiety. Organic illnesses such as hypertension, diabetes, myocardial infarction, and osteoarthritis were present in 16 patients. The dosage was 1 tablet twice daily reduced to 1 tablet daily in 5 instances. Treatment lasted an average of five weeks except in 2 patients in whom it was discontinued early because of side-effects. Complete relief of symptoms and acquisition of a better understanding of problems occurred in 24 patients. Substantial relief of symptoms and some insight into their problems occurred in 23 patients. The result was poor, with no improvement in insight in 8 patients. Benefit when it occurred usually was apparent in ten to fourteen days, and consisted of disappearance of fatigue, return of normal sleep pattern and appetite, renewed interest in outside activities, increased decisiveness, elimination of tenseness and nervousness, and freedom from psychosomatic complaints. The combination did not affect the course of any organic illness, but brought a good to excellent result in 13 of the 16 patients with organic disease. Only 3 of the 14 patients who were past the age of 60 years failed to respond. Side-effects consisted of insomnia in 2 patients which disappeared spontaneously or when the drug was discontinued, drowsiness in 1, increase in blood pressure in 1, and decrease in blood pressure in 1 patient.

ADENOACANTHOMA OF THE ENDOMETRIUM. A REPORT OF 24 CASES AND A REVIEW OF SQUAMOUS METAPLASIA.

Marcus, S. L. *Am. J. Obst. & Gynec.* **81:** 259 (Feb.) 1961.

The term "adenoacanthoma of the endometrium" should be reserved for an adenocarcinoma with extensive squamous metaplasia. Specific studies on this lesion are rare, and diametric opinions exist on several aspects, including the prognosis compared to the ordinary endometrial carcinoma. The squamous cells in adenoacanthoma are similar to the metaplastic change manifest in various benign endometrial conditions in the human subject and in experimental lesions in animals. The mature, well-differentiated squamous cells appear to arise from basal cells derived from the glandular epithelium as a regenerative

response to injury. Twenty-four adenoacanthomas were noted in a review of 348 endometrial carcinomas—an incidence of 6.8 per cent. A high incidence of nulliparity and a tendency toward a late menopause were noted, both of which have also been reported in patients with pure endometrial carcinoma. All but one of the lesions were well-differentiated adenocarcinomas. Compared to those in previous studies of pure endometrial carcinoma, these cases presented a significantly higher incidence of extension to the cervix. No significant difference was noted, however, in the incidence of myometrial invasion or metastasis to the vagina, ovaries, or tubes. Hysterectomy and bilateral salpingo-oophorectomy was the treatment in 17 patients; preoperative irradiation and operation in 5 patients; and irradiation alone in 2 patients. In 16 patients eligible for five-year follow-up, the survival in all 3 groups was 75 per cent—a figure comparable to the survival rate in cases of pure endometrial carcinoma. It therefore seems that there is no basis for the diametric statements that patients with adenoacanthoma have a significantly better or poorer prognosis than those with pure endometrial carcinoma. It would appear that the prognosis in adenocarcinoma of the endometrium is unaltered by the presence of squamous metaplasia. (From author's summary.)

RELATION OF ELECTROENCEPHALOGRAM TO BLOOD PRESSURE IN ELDERLY PERSONS.
Obrist, W. D.; Busse, E. W., and Henry, C. E. *Neurology* **11:** 151 (Feb.) 1961.

The relation between clinical electroencephalographic findings and blood pressure was investigated in 233 psychiatric patients and 261 mentally normal controls past 60 years of age. Among the former, there was a greater number of normal electroencephalograms at high blood pressure levels and more abnormal electroencephalograms at low levels. Not all types of abnormality were associated to the same degree with blood pressure; only tracings with diffuse slow activity (with or without focal accentuation) showed an appreciable correlation. The incidence of excess fast activity or focal slowing varied only slightly with blood pressure. A similar correlation was not obtained in control subjects who showed considerably less diffuse slow activity. It is suggested that diffuse slow activity in aged psychiatric patients results from the combination of a relatively low blood pressure and cerebral arteriosclerosis. A significant number of psychiatric patients in this study had reduced blood pressure in the presence of cardiovascular disease. The control subjects on the contrary tended to have elevated blood pressure in association with signs of arteriosclerosis. These findings suggest that impaired cerebral blood flow is the crucial variable underlying diffuse slow wave abnormalities in aged psychiatric subjects.

RECURRENT EPISODIC BLINDNESS IN CRANIAL ARTERITIS.
Pan, A.; Little, S., and Rogers, A. G. *Canad. M. A. J.* **84:** 108 (Jan. 14) 1961.

The presence of cranial (temporal) arteritis should be suspected in any patient 55 years of age or older with headache of recent onset and an associated high sedimentation rate. A case is presented in which episodic blindness associated with cranial arteritis occurred 46 times, 38 times in the left eye and 8 in the right eye. These episodes of amaurosis fugax occurred only after angiography but the reason for this is not known. On several occasions at the onset of the attacks, the patient complained of seeing scintillations of colored lights. Spasm of the retinal branches occurred on many occasions during an attack. The retinal veins became engorged and fragmented into segments. Amyl nitrite did not abort the attacks of visual loss and antibiotics did not lower the patient's temperature. Cortisone, however, dramatically relieved headache and reduced the temperature to normal. The temporal arteries became softer and reduced in size five days after the institution of cortisone therapy. The dosage was 300 mg. the first day, reduced to 225 mg. daily four days after the first attack of blindness. It gradually was reduced to a maintenance dose of 75 mg. and then to 37.5 mg. per day without a recurrence of attacks of visual loss or headache. Amaurosis fugax continued for eleven days after cortisone was commenced. Temporal arteritis usually affects persons 55 years of age and over. Its etiology is not known but it is generally

regarded as a collagen disease. It affects all layers of the arterial wall. The onset usually is insidious but it may be sudden. Preceding the headache, there may be a period of weeks or months of malaise, anorexia, fatiguability, weakness, weight loss, night sweats, dizziness, vague pains in muscles and joints, dyspepsia, and a low fever. A mild, normocytic anemia may be present. The sedimentation rate always is increased. There is usually a mild to moderate leukocytosis with polymorphonuclear neutrophils predominating. The headache is usually severe and constant with associated hyperalgesia of the scalp. Ocular complications occur in 40 per cent of cases. When there is ocular palsy, it usually occurs after the onset of headache. Signs of cerebral damage and encephalitis may be present during the acute stage of the disease. Cranial arteritis is a self-limited disease which runs its course in two to thirty months. Relapses occur but most patients recover. Treatment consists of the administration of corticosteroids which bring about subjective relief of local and systemic symptoms, reduce the fever and sedimentation rate, and prevent blindness. Cortisone therapy should be started as soon as the diagnosis is suspected. The sedimentation rate may remain high for a long while and, if it does, vision is threatened. Cortisone must be continued, therefore, until the disease has run its course. Some investigators have used anticoagulants concurrently to prevent possible intravascular thromboses in the artery affected.

CIRRHOTIC HEART FAILURE.

Paton, A., and Thompson, J. W. *Brit. M. J.* **1:** 179 (Jan. 21) 1961.

Three cases are presented of cardiac failure believed to be secondary to portal cirrhosis. They presented with dyspnea and peripheral edema. The diagnosis of cardiac failure was supported by a high output state and by finding generalized venous congestion at necropsy. Diuretics, salt restriction, and bed rest failed to influence the edema in these patients. The removal of edema fluid appeared to hasten death. The literature furnishes evidence that severe liver disease can lead to hemodynamic changes, so that cardiac failure might be expected to occur. Diagnosis may be subject to error because of a tendency to attribute the cardiac failure to cor pulmonale, especially in men, or to valvular disease. The gross edema may suggest constrictive pericarditis, but the quiet cardiac impulse and the low output should serve to distinguish it. Jaundice may be slight or absent, but when it is present, it may be attributed to venous congestion. Other evidence of liver disease may be masked by anasarca but careful search may reveal signs such as fetor hepaticus or a coarse tremor. Prompt recognition is essential. Since standard measures of treatment for cardiac failure are of no avail in this situation, and removal of edema fluid mechanically has a disastrous effect, more effective measures must be sought. Attempts to improve body proteins (in the absence of clinical evidence of liver failure) may succeed, or methods of promoting diuresis, such as the use of steroids or spironolactones and osmotic diuretics, may be justified.

PROLAPSE OF THE IRIS IN SENILE CATARACT EXTRACTION AND ITS PREVENTION.

Pflüger, E. *Klin. Monatsbl. Augenheilk.* **35:** 332, 1897; translated by Young, C. A., Jr. and Diettrich, H-G. *South. M. J.* **54:** 61 (Jan.) 1961.

Simple extraction for cataract might previously have been the preferred operation for senile cataract were it not for the occurrence of prolapse of the iris. Its advantages include greater integrity of the eye, a perfect optical system, less frequent injection, decreased incidence of irritation of the iris, smoother and faster wound healing, almost complete absence of hemorrhage during operation, and the absence of glaucoma following it. The causes for prolapse of the iris are: 1) hypermaturity or immaturity of the cataract, 2) the technic of operation, and 3) the general health and reactivity of the patient. Hypermaturity of the cataract may make simple extraction impossible, so that it has to be removed in the capsule by a spoon or loop. Portions of cortex that cannot be removed completely sometimes cause prolapse of the iris through swelling. A large-flap technique makes lens

delivery easy and is essential to simple extraction. A generous opening in the capsule and correct maneuvering for direct expulsion are important. An attempt should be made to rotate the lens around its horizontal axis by applying pressure directed posteriorly to the lower margin of the lens. The rotation must be sufficient to allow the lens equator (directed forwards) to pass the pupil within the eye. The use of a speculum with a spoon movable around an axis has decreased the occurrence of prolapse of the iris. The anterior chamber must be cleared of cortex because of the danger of delayed swelling with secondary iris prolapse and membrane formation. If a patient is tense and frightened, he can push his iris out. Even deep anesthesia does not protect against prolapse of the iris or postoperative hemorrhage. The presence of circulatory disturbances, chronic cough, and acute psychoses do not favor simple extraction. Prolapse of the iris can be avoided if simple extraction is practiced only with proper indications. It is usually preferable to try to preserve the round pupil and let the lens be delivered through it. Iridectomy frequently will be necessary afterward, but this procedure will not always protect against prolapse of the iris. It is most likely to occur when lens material remains in the capsule, or when the patient does not remain quiet. Pflüger makes a small peripheral iridectomy. The small hole allows aqueous to pass if the wound should separate, and functions as a safety vent. This procedure added to simple flap extraction combines the advantages of the simple extraction with those of a combined extraction, yet avoids its inconveniences. The pupil remains intact and usually becomes smaller because of the relatively greater strength of the sphincter opposite the peripheral iridectomy. There will be a better optical "set-up" and less postoperative astigmatism than with the combined procedure. The inferiorly displaced upper margin of the pupil combined with the hole in the iris gives protection against glaucoma. The primary advantage is prevention of incarceration of the iris. The technique for peripheral iridectomy usually is: lens delivery, iris reposited if it has not retracted spontaneously, anterior chamber cleaned, eye cleared, fixation and speculum removed; the patient has sat up and passed the finger test for vision. Then, with the upper lid elevated with the finger, an iris forceps is directed toward the iris root, a small peripheral piece pulled out, and snipped off. Should the patient move, refixation of the globe may become necessary.

OBSERVATIONS ON THE MANAGEMENT OF RHEUMATOID ARTHRITIS AND RELATED DISORDERS WITH THE NEWER CORTICOSTEROIDS.

Robins, H. M. *New York J. Med.* **61:** 717 (March 1) 1961.

The judicious use of corticosteroids in the treatment of rheumatoid arthritis and related disorders implies an awareness to the marked variations which exist in individual response to any one analogue, as well as of certain qualitative differences between these agents in therapeutic and in unwanted effects. A comparative experience with prednisone, methylprednisolone, triamicinolone, and dexamethasone confirmed the impression, gained from an accumulating wealth of clinical material, that, as an antirheumatic agent, no single corticosteroid compound is consistently or convincingly superior in all categories of effect to any other corticosteroid. With regard to the compound, or optimal dosage schedule, arbitrary recommendations are unrealistic. An empiric approach to the administration of these potent substances is suggested for the achievement of therapeutic benefits with a minimum of unwanted physiologic reactions. A proper choice of the patient, a supplemental therapy with other appropriate measures, and a strict medical supervision contribute to the success of a long-continued program in the management of chronic disorders. When 63 patients with various arthritic disorders were given prednisone, methylprednisolone, triamcinolone, or dexamethasone in varying treatment programs, the highest percentage of good to excellent responses was achieved with triamcinolone at the dosage level employed. However, a firm impression was obtained that the antirheumatic influence of all of the newer corticosteroids was ample when enough medication could be administered without inducing serious reactions. Triamcinolone was preferred in cases of arthritis with

psoriasis because of an exceptional ability to clear the skin. Other distinguishing effects were these: with prednisone—a greater frequency of gastro-intestinal symptoms, ecchymosis, and euphoria; with dexamethasone—a voracious appetite accompanied by a rapid gain in weight and edema requiring treatment with diuretic agents; with methylprednisolone—leg cramps; and with triamcinolone—a reversible weight loss associated with muscle weakness. (From author's summary.)

ARTERITIS IN RHEUMATOID ARTHRITIS.

Schmid, F. R.; Cooper, N. S.; Ziff, M., and McEwen, C. *Am. J. Med.* **30:** 56 (Jan.) 1961.

The clinical and pathologic features of 17 patients with rheumatoid arthritis and histologically proved arteritis were examined and compared with the data in 14 other patients with arthritis who had negative biopsy findings. Of the 17 patients with arteritis, 11 had a necrotizing lesion. The reports of an additional 81 patients with arteritis, described in the literature, were surveyed for comparison with those of the present study. Several findings were more commonly associated with the patient with necrotizing arteritis. These included a higher incidence of episcleritis, peripheral neuritis, and the serum L.E. factor. The presence of these findings is suggestive evidence of necrotizing arteritis. Subcutaneous nodules and clinically diagnosed pericarditis were noted equally in patients with either type of arteritis, but infrequently in the patients in whom the results of biopsy were negative. No precipitating factors for arteritis were found. Evidence for the suggestion that the use of corticosteroids is related to this complication is not convincing, although more cases of necrotizing arteritis have been reported in the era after cortisone; the data lend some support to the suggestion that in some patients corticosteroid may promote transformation of non-necrotizing to necrotizing arteritis. The data do not finally answer the question whether arteritis, especially of the necrotizing type, is a fundamental event in the pathogenesis of arthritis or, alternatively, that arteritis and arthritis are diverse manifestations of rheumatoid disease. (From author's summary.)

ROLE OF THE NEWER URICOSURIC AGENTS IN MANAGEMENT OF GOUT.

Seegmiller, J. E. *Bull. Rheum. Dis.* **11:** 241 (Feb.) 1961.

Sulfinpyrazone (Anturan) and zoxazolamine (Flexin) are uricosuric agents which inhibit the tubular reabsorption of urate in the kidney and possess approximately equivalent potency. The response to sulfinpyrazone is greater than that to phenylbutazone or probenecid. It causes side-effects consisting primarily of gastro-intestinal distress, peptic ulcer, renal colic, and urticaria. Zoxazolamine exerts its uricosuric effect at a much lower dosage than when it is used as a muscle relaxant. Side-effects associated with it include gastro-intestinal discomfort, rarely urticaria, and a transient nephritis. The action of these drugs is additive and it is antagonized by low doses of salicylate. Aspirin and other salicylate-containing drugs should be avoided while these substances are being administered. These uricosuric agents are useful in hypertensive patients in whom urate retention has been caused by chlorothiazide or hydrochlorothiazide. For the treatment of acute gouty arthritis, colchicine remains the best agent for prophylaxis, to abort impending attacks, and to terminate fully developed attacks. ACTH (100 units) in long-acting repository form is effective in terminating acute attacks of gout. Phenylbutazone also will terminate an acute attack of gout and is useful in stubborn cases with recurrent attacks despite temporary response to colchicine. The response to steroids is less consistent than that to other agents and attacks are likely to recur upon discontinuation of the steroid. In the case of tophaceous gout, the serum urate levels are higher than in patients with no deposits. The deposits can be resolved by lowering the serum urate level to normal or nearly normal. This should also reduce the frequency and severity of attacks. Indications for therapy with a uricosuric agent include: 1) the presence of tophi; 2) gout with a serum urate level con-

sistently above 8 mg. per 100 ml.; and 3) frequent attacks of gout despite the maximal daily dose of colchicine that can be tolerated. Uricosuric agents are not of value in treating acute gouty arthritis and their frequent use may lead to increased frequency of attacks of gout. They must, therefore, be introduced during a quiescent period and 1 to 2 mg. colchicine given concomitantly. The potent uricosuric agents carry the hazard of deposition of urate in the urinary tract. This can be prevented by a high fluid intake, moderate alkalization of the urine, and the use of low doses initially and administration in fractional doses throughout the day. The initial dosage of sulfinpyrazone is 50 mg. twice daily. The number of doses is gradually increased, and then the size of the dose, to 100 mg. four times daily over a two-week period. The initial dosage of zoxazolamine is 65 mg. twice daily, with a gradual increase over the same period to 125 mg. four times daily. The objective is to produce a serum urate level below 6 mg. per 100 ml. The level should be checked during therapy and the maintenance dose adjusted according to the needs of the patient. In the presence of renal impairment, larger doses will be required or a combination of the two drugs. A conservative approach to diet calls for a low-purine diet until the gout has been controlled with regard to acute attacks and serum urate levels.

HORMONAL THERAPY IN CANCER OF THE BREAST. XVII. THE EFFECT OF ANDROSTERONE ON CLINICAL COURSE AND HORMONAL EXCRETION.

Segaloff, A.; Weeth, J. B.; Rongone, E. L., and Bowers, C. Y. *Cancer* **14:** 195 (Jan.–Feb.) 1961.

The test subjects were 22 patients with advancing metastatic disease, all of whom were at least one year postmenopausal or had been castrated, and who were divided into groups according to menopausal status and according to the dominant system involved: local or soft-tissue disease, osseous disease, or visceral disease. Androsterone in saline suspension was administered intramuscularly in doses of 100 mg. three times per week; 50 mg. was given daily during urine collections. Only 1 patient responded. In this patient with dominant visceral involvement, during two months of therapy the primary and axillary lesions regressed, central nervous system symptoms cleared slightly, but there was no change in osteolytic lesions. Regression occurred during inadvertent discontinuation of therapy and the lesions could not again be controlled when therapy was reinstituted. The only significant change in excretion pattern occurred in the 17-ketosteroids, which rose an average of 9.3 mg. per twenty-four hours. No significant changes took place in the excretion of other steroids, gonad-stimulating hormone, or prolactin. None of the patients manifested polycythemia. In one patient in whom serum cholesterol levels were measured before and after treatment, the average fell from 409 to 113 mg. per 100 ml. Only slight evidence of virilization occurred in a few patients. Its absence was due in part to the ineffectiveness of therapy and consequent short-term administration.

INTERSTITIAL CYSTITIS: AN EXPLANATION FOR THE BENEFICIAL EFFECT OF AN ANTIHISTAMINE.

Simmons, J. L. *J. Urol.* **85:** 149 (Feb.) 1961.

The normal bladder wall was found to contain mast cells throughout. They were concentrated in connective tissue, particularly between muscle bundles and in the perivascular area. The bladder wall also had a histamine content that varied from 0.96 to 7.4 gamma per gram of tissue in the specimens examined. The histamine was evenly distributed. In one case of ulcers of the bladder, the mast-cell content was increased in the bladder wall without a corresponding rise in the histamine content. It is suggested that many of the pathologic changes in the bladder wall in interstitial cystitis are secondary to the presence of mast cells and to the local release of histamine. Thus, the release of histamine by mast cells may initiate or perpetuate edema throughout the bladder wall. Because of this release there will be increased capillary permeability, protein leakage, marked edema, and stasis.

As the edema continues, mast cells may contribute hyaluronic acid in addition to the mucopolysaccharides supplied by the fibroblasts with resulting fibrosis. With continued fibrosis and scar formation, mucosal ulceration will occur. Six cases of interstitial cystitis are reported in which the patients responded to the administration of antihistamine. The duration of the response proved variable. Cystoscopy showed no change in the appearance of ulcers in the bladder during this therapy.

ON THE EFFECT OF ATHEROSCLEROSIS AND GOITRE ON AORTIC HISTOPATHOLOGY AND MUCOPOLYSACCHARIDE CONTENT.

Uotila, U.; Levonen, E., and Raekallio, J. *Acta endocrinol.* **36:** 1 (Jan.) 1961.

The effect of goiter on aortic mucopolysaccharides in sclerotic and nonsclerotic subjects was studied by histologic and biochemical methods. Atherosclerosis alone lowers the quantity of aortic acid mucopolysaccharides. Goiter alone shows a tendency to increase the mucopolysaccharide content of the aorta. Goiter accelerates the effect of atherosclerosis in decreasing the aortic mucopolysaccharides, *i.e.*, a fibrosing and sclerosing effect. Histologic observations reveal that atherosclerosis is characterized, in all groups, by fatty degeneration of the intima and inner elastic membrane and destruction of the elastic connective tissue; in the process of repair the mucopolysaccharides increase. In connection with the ensuing collagenization, the mucopolysaccharides decrease. It is suggested that goiter, by hypo- or hyperfunction, causes metabolic disturbances in the aortic wall and thus promotes atherosclerosis. (From authors' abstract.)

MANAGEMENT OF RECTUM AND RECTOSIGMOID CANCER IN ELDERLY PATIENTS.

Welborn, M. B. *J. Indiana M. A.* **54:** 36 (Jan.) 1961.

Among 178 patients with malignant lesions of the anus, rectum, or rectosigmoid seen in a twelve-year period, 95 were 65 years of age or older. Treatment carried out was as follows in the numbers of patients stated: single-stage combined abdomino-perineal resection, 34; two-stage combined abdominoperineal resection, 2; three-stage exteriorization procedure, 1; anterior resection, 12; radical local excision with inversion of the distal rectal segment, 8; transcolonic excision of a malignant polyp, 2; palliative colostomy, 3; laparotomy with biopsy, 9; posterior excision with colostomy, 1; radical local excision by transrectal approach, 7; proctoscopy with biopsy only, 6; external irradiation only, 2; medical treatment, 7; and no treatment (death soon after admission), 1. Combined abdominoperineal resection was performed in 36 of the older age group and in 43 patients under age 65. There were 3 deaths in the former group and 4 in the latter—an over-all hospital mortality rate of 8.8 per cent. The rates for older and younger age groups were approximately the same. The mortality rate compared favorably with that for other major surgical procedures in elderly persons. These statistics indicate that radical surgery can be carried out with care when necessary in patients with obstruction, hemorrhage, and tenesmus. Each rectal malignant lesion has its own biologic character, but these tend to be indolent, slowly growing tumors with a low invasive potential. Although radical surgery may be the best method of treatment, a small group of patients may have to be managed more conservatively. Radical local excision for anatomically small, superficial lesions alone or combined with fulguration or irradiation may prove satisfactory in these.

NEWS AND NOTICES

THE AGING PATIENT

In recognition of the fact that the medical care of elderly patients is occupying an increasing portion of the practice of most physicians, current knowledge of aging and the aging patient was recently reviewed by a panel of physicians and scientists. Topics covered during the discussion ranged from the therapeutic and dietary needs of the older patient to special examination and diagnostic procedures.

Participating in the discussion were: Dr. Geoffrey H. Bourne, Professor and Chairman of the Department of Anatomy, Emory University, Atlanta, Georgia, moderator; Dr. Joseph T. Freeman, President of the Gerontological Society, Inc. and an internal medicine specialist, Philadelphia, Pennsylvania; Dr. Albert R. Behnke, Jr., Director of the Institute of Applied Biology, Presbyterian Medical Center, San Francisco, California; Dr. Nathan W. Shock, Chief, Gerontology Branch, National Heart Institute, National Institutes of Health, Baltimore, Maryland; Dr. Joseph H. Gerber, Director, and Dr. Stanley R. Mohler, Medical Officer, Center for Aging Research, National Institutes of Health, Bethesda, Maryland.

Copies of the text of THE AGING PATIENT—the recording made of this session by the *Voice of Medicine*, the recorded medical journal of the Excerpta Medica Foundation—are available free upon request to: Information Officer, Center for Aging Research, Division of General Medical Sciences, National Institutes of Health, Bethesda 14, Maryland.